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CASE REPORT

A Rare Case of Dual Clonal B-Cell Hairy Cell Leukemia: Diagnostic Challenges

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SUMMARY

Background: **Hairy Cell Leukemia (HCL) is a rare chronic B-cell disorder characterized by cytopenia, splenomegaly, and bone marrow infiltration. A 42-year-old female presented with gingival swelling and bleeding, later diagnosed with HCL involving lymph nodes, liver, and spleen.**
Methods: **The patient underwent blood tests, PET-CT, bone marrow flow cytometry, biopsy, and lymph node aspiration, confirming HCL. Notably, flow cytometry revealed dual clonal B-cell populations, both CD5-negative and CD10-negative. Immunohistochemistry showed positive B-cell markers (CD20, CD23) and BRAF-V600E mutation. Cladribine chemotherapy began on April 18, 2022, followed by supportive treatment.**
Results: **Blood tests showed pancytopenia, and PET-CT indicated lymph node, spleen, liver, and bone marrow involvement. Bone marrow biopsy confirmed HCL with fibrosis. The patient experienced bone marrow suppression during chemotherapy and received supportive care, eventually leading to a successful discharge.**
Conclusions: **HCL is a rare B-cell malignancy causing pancytopenia and organ involvement. The identification of dual clonal B-cell populations is crucial for accurate diagnosis. Early diagnosis and cladribine chemotherapy are effective. Immunohistochemical and genetic testing are key for diagnosis and treatment planning.**
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KEYWORDS

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INTRODUCTION

Hairy cell leukemia (HCL) is a rare B-cell lymphoproliferative disorder characterized by the presence of lymphocytes with distinctive cytoplasmic projections that resemble hair, hence the name [1]. HCL accounts for approximately 2% of all lymphoid leukemias and primarily affects middle-aged individuals, with a male predominance [2]. It is often characterized by pancytopenia, splenomegaly, and infiltration of the bone marrow by malignant cells [3]. The pathogenesis of HCL involves the BRAF V600E mutation, which is present in the vast majority of cases and plays a critical role in the disease's progression [4]. Despite being a chronic disease, effective treatments such as cladribine have led to significant improvements in patient outcomes, with high

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rates of durable remission [5].

The diagnosis of HCL can be challenging, especially in cases with atypical presentations, such as extensive lymphadenopathy or involvement of extranodal sites [6]. This report describes a case of HCL in a 42-year-old female with widespread lymphadenopathy, hepatosplenomegaly, and secondary bone marrow fibrosis. The case highlights the importance of integrating clinical, radiological, and histopathological findings to reach an accurate diagnosis and initiate timely treatment.

CASE PRESENTATION

A 42-year-old female presented to our hospital with complaints of gingival swelling and bleeding for one week. On admission, laboratory studies revealed the following: white blood cell count (WBC) of 2.16 x 10^9/L (decreased), neutrophil count of 0.59 x 10^9/L (decreased), lymphocyte count of 1.56 x 10^9/L, monocyte count of 0.01 x 10^9/L (decreased), eosinophil count of 0.00 x 10^9/L (decreased), hemoglobin of 72 g/L (decreased), platelet count of 33 x 10^9/L (decreased), and reticulocyte count of 41.1 x 10^9/L with reticulocyte percentage of 1.55%.

Whole-body PET-CT conducted on April 8, 2022, showed: 1) bilateral cervical, supraclavicular, mediastinal, porta hepatis, retroperitoneal, and intra-abdominal lymphadenopathy with increased FDG uptake, highly suggestive of lymphoma involvement; 2) hepatosplenomegaly with abnormal FDG uptake, suggesting lymphoma infiltration; 3) FDG-avid lesions in bilateral humeri, pelvis, and femurs, consistent with lymphoma involvement; 4) bilateral axillary lymph nodes showing inflammatory hyperplasia; 5) bilateral pleural effusions and mild inflammatory changes in both lungs; 6) hepatic cyst and right renal cyst.

Flow cytometry analysis demonstrated CD5-CD10-CD19+Kappa+ mature monoclonal B-cells (15.89%), and an additional population of CD5-CD10-CD19-CD22+CD20+CD23+fmc7+Kappa+ monoclonal B-cells (12.56%) (Figure 1). Bone marrow aspiration showed an increased lymphocyte proportion, with some cells exhibiting characteristic "hairy" cytoplasmic projections (Figure 2). Bone marrow biopsy revealed hypercellularity (approximately 90%) with lymphoid hyperplasia, moderate-sized cells with clear cytoplasm, prominent nucleoli, and reticulin fibrosis (MF-2). Histopathological examination indicated a diagnosis of CD5-negative, CD10-negative B-cell lymphoma with secondary marrow fibrosis, consistent with hairy cell leukemia. Lymph node fine needle aspiration biopsy of the left cervical lymph node suggested a small B-cell lymphoma/leukemia, favoring hairy cell leukemia. Immunohistochemistry showed positivity for CD20, CD79a, CD23, BCL2 (90%), and CyclinD1 (weak), while negative for CD3, CD5, CD10, SOX-11, and others. BRAF V600E mutation was detected, supporting the diagnosis of HCL.

The patient was diagnosed with hairy cell leukemia, Ann Arbor-Cotswolds Stage IV A, with secondary bone marrow fibrosis. The patient received cladribine chemotherapy (8.82 mg qd, days 1 - 5) starting on April 18, 2022. During post-chemotherapy myelosuppression, supportive treatment included granulocyte colony-stimulating factor (G-CSF) to stimulate white blood cell production and transfusions as needed. The patient was discharged in stable condition following symptomatic improvement.

DISCUSSION

Hairy cell leukemia (HCL) is a rare but distinct form of B-cell lymphoproliferative disorder that can present with unique clinical features, including splenomegaly, cytopenias, and bone marrow involvement [7]. The diagnosis of HCL can be challenging, particularly in cases with atypical manifestations, such as significant lymphadenopathy and hepatosplenomegaly [2]. In this patient, the presence of systemic lymphadenopathy and increased FDG uptake seen on PET-CT initially suggested the possibility of a more aggressive lymphoma, necessitating a comprehensive diagnostic approach [3].

The histopathological and immunophenotypic findings in this case were essential in establishing the diagnosis of HCL, particularly highlighting the presence of dual clonal B-cells. Flow cytometry revealed two distinct populations of CD5-negative, CD10-negative monoclonal B-cells, indicating dual clonal B-cell involvement. This finding, along with the identification of the BRAF V600E mutation, was consistent with HCL [4]. The BRAF V600E mutation is present in approximately 90% of HCL cases and has become an important diagnostic and therapeutic target [8]. The identification of this mutation in our patient not only confirmed the diagnosis but also provided a potential avenue for targeted therapy if needed in the future [9].

Bone marrow fibrosis is a common finding in HCL, which often results in a "dry tap" during bone marrow aspiration, further complicating the diagnostic process. In this case, bone marrow biopsy revealed hypercellularity and fibrosis (MF-2), consistent with HCL. The presence of extensive bone marrow infiltration and fibrosis contributed to the cytopenias seen in this patient. Additionally, the presence of systemic lymphadenopathy, which is relatively uncommon in classic HCL, highlighted the need for a differential diagnosis that included other forms of B-cell lymphomas, such as splenic marginal zone lymphoma or mantle cell lymphoma [10]. However, the immunophenotypic profile and BRAF mutation status were definitive for HCL [11]. The use of cladribine as the initial treatment for this patient aligns with current standard of care for HCL [12]. Cladribine, a purine analog, has been shown to induce durable remissions in the majority of patients with HCL, often with a single cycle of treatment. In this case, the patient responded well to cladribine, with res-

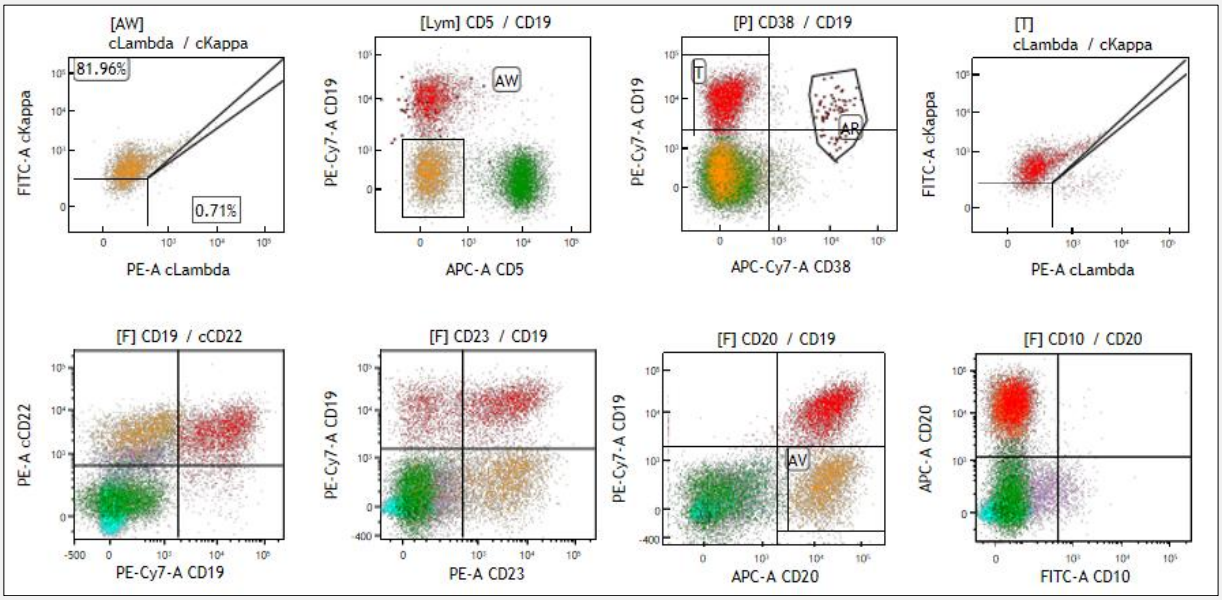

Figure 1. The flow cytometry results show approximately 15.89% CD5- CD10- CD19+ mature monoclonal B lymphocytes, and approximately 12.56% CD5- CD10- CD19- mature monoclonal B lymphocytes.

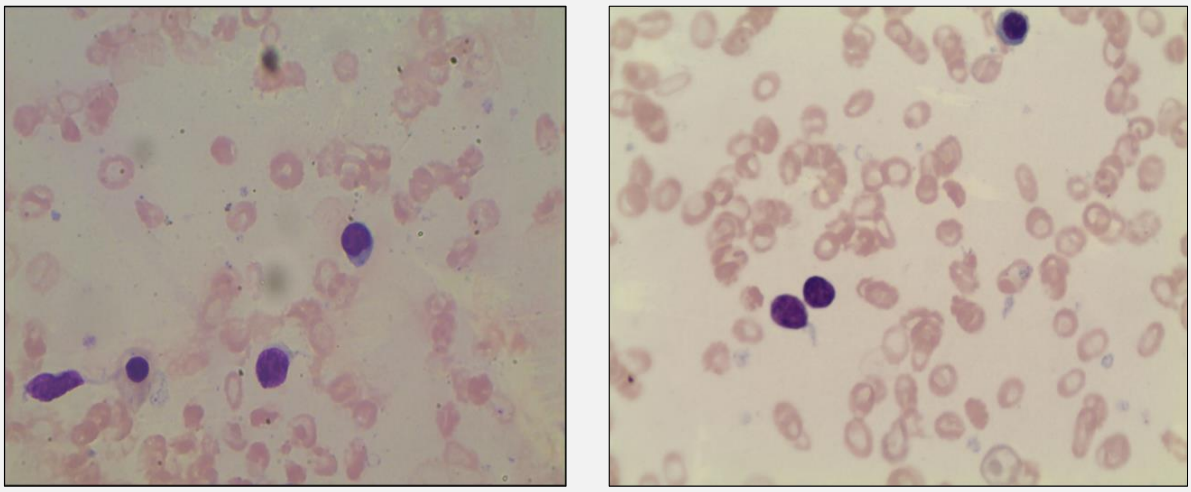

Figure 2. Bone marrow cytomorphology indicates an increased proportion of lymphocytes, with some lymphocytes displaying cytoplasmic tailing and spiculated (burr-like) projections.

olution of symptoms and improvement in blood counts. The post-treatment myelosuppression, managed with G-CSF and supportive care, is a well-recognized complication of cladribine therapy but is generally transient [13].

This case underscores several important aspects of HCL

management [14]. First, it highlights the importance of considering HCL in the differential diagnosis of patients presenting with cytopenias, lymphadenopathy, and hepatosplenomegaly. Second, it demonstrates the utility of integrating clinical findings with advanced diagnostic techniques, such as flow cytometry and molecular testing for BRAF mutations, to accurately diagnose HCL. Finally, the favorable response to cladribine observed in this patient reaffirms the efficacy of purine analogs in achieving remission in HCL.

Despite its rarity, HCL remains a highly treatable condition, with most patients achieving long-term remission following appropriate therapy. However, challenges remain, particularly in cases with atypical features or relapsed/refractory disease. Future research should focus on optimizing treatment regimens, exploring targeted therapies, and improving diagnostic accuracy, particularly in patients with unusual presentations.

CONCLUSION

This case underscores the importance of integrating clinical, radiological, histopathological, and flow cytometry findings in diagnosing HCL. Flow cytometry, in particular, was crucial in identifying the dual clonal B-cell populations, highlighting its importance in diagnosing this rare and challenging form of hairy cell leukemia. Early diagnosis and appropriate therapy can significantly improve prognosis. Further studies are needed to better understand the pathophysiology and optimal treatment approaches for this rare disease.

Declaration of Interest:

All authors declare that there are no conflicts of interest.

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