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Case Report

Hairy Cell Leukemia with Marrow Reactive Plasmacytosis and Mast Cell Hyperplasia: A Case Report and Brief Review of the Literature

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Abstract
Hairy cell leukemia (HCL) and HCL-like disorders, including HCL-variant, are disorders of heterogeneous mature lymphoid B-cells known for their hairy cell infiltration accompanied by a specific genetic profile, various clinical presentations, and, as they are uncommon hematological malignancies characterized by pancytopenia, the need for appropriate therapy. Sometimes HCL creates diagnostic challenges for clinicians, and its coincidence or association with mast cell and plasma cell infiltration is a rare condition. Herein, we report a case of HCL with confusing manifestations. A 44-year-old man was referred to the hospital for weakness, fatigue, and watery, non-bloody diarrhea. The laboratory tests showed pancytopenia, leading to a referral for bone marrow aspiration and biopsy. Medium to large cells exhibiting widespread cytoplasm, oval nuclei similar to monocyte nuclei (kidney-shaped) accompanied by an increased number of mast cells, and plasma cells were observed in the biopsy sample. In flow cytometry, the neoplastic cells were positive for CD19, FMC7, and the co-expression of the CD20/CD25, CD11C/CD22, and CD103 markers. In immunohistochemical staining, the mast cells were positive for CD117, the plasma cells were positive for CD138, and the hairy cells were positive for CD20. Overall, hematopathologists must be aware of various morphologic confounding factors such as lack of typical cell morphological features and increased plasma cell and mast cell infiltration in the diagnosis of patients with HCL.
Keywords: Hairy cell leukemia, Mast cell, Plasma cell

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Introduction

Discovered in 1923 and further characterized in 1958, hairy cell leukemia (HCL) and also HCL-like disorders, such as HCL-variant, are heterogeneous disorders of mature lymphoid B-cells known for the infiltration of hairy cells along with a specific genetic profile and various clinical presentations; they are uncommon hematological malignancies characterized by pancytopenia and the need for appropriate therapy (1-3). Diagnosis of HCL is made using the morphological characteristics of hairy cells and according to the expression of CD11, CD123, CD103, and CD25, in addition to trephine biopsy, which makes it possible to determine the degree and pattern of infiltration (solid, interstitial, or diffuse) and also the presence of the BRAF V600E somatic mutation (4-6). The diagnosis of atypical HCL is challenging for clinicians, and its coincidence or association with mast cells or plasma cells is a rare condition, making diagnosis and treatment more challenging (7-10). Herein, we reported a case of HCL with confusing manifestations.

Case Presentation

A 44-year-old man was admitted to the hospital for weakness, fatigue, and watery non-bloody diarrhea in the previous three weeks. The laboratory tests showed pancytopenia leading to a referral for bone marrow aspiration and biopsy. Medium to large cells with widespread cytoplasm and oval nuclei similar to monocyte (kidney-shaped) nuclei accompanied by an increased number of mast cells and mature plasma cells (about 15%) were detected (Figure 1). There were no hairy projections on the surface of the cell cytoplasm, and the chromatin was homogenous, so plasma cell dyscrasia was suspected based on morphologic findings. Bone marrow biopsy slides stained with Giemsa also showed an increase in the mast cell population. The edge of the

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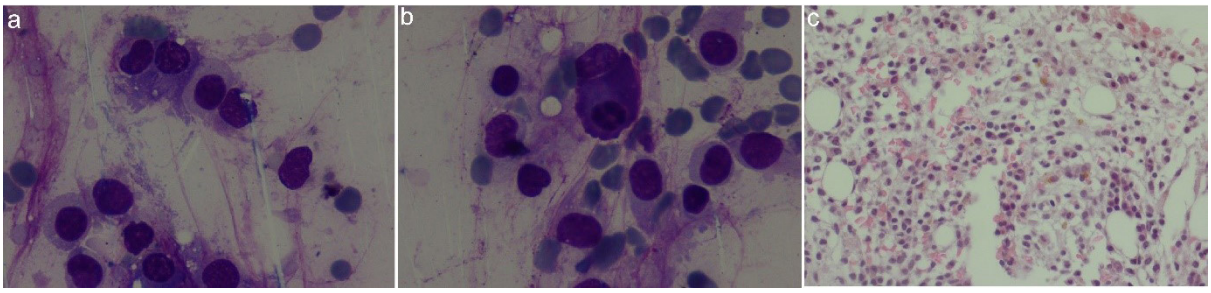

Figure 1. (a)&(b) Bone marrow aspiration (Giemsa stain ,×1000):and (c) Bone marrow biopsy (H&E stain , ×100): medium sized lymphoid cells with oval or kidney-shaped nuclei accompanied by an increased number of mast cells and plasma cells.

spleen was palpated in clinical examination, and a mobile 0.5×0.5 cm^2 submandibular gland was detected. There were two ecchymosed regions in the neck. Laboratory investigations revealed 1200/mm^3 leukocyte count, 6.4 g/dL hemoglobin, 4000/mm^3 platelet count, 125 µg/dL serum iron, 436 IU/L LDH, 330 ng/mL ferritin, 119 ESR mm in first hour, and increased CRP. In serum electrophoresis, increased gamma-globulin was noted, and IgA and IgG were found to be increased (IgG: 18.46 (normal range: 6.58–18.37) g/L; IgA: 5.8 (normal range: 0.71–3.6) g/L) with normal levels of IgM and IgE. In urinalysis, there was no proteinuria, and the result of the Bence-Jones protein test was negative. In ultrasonography, the spleen was enlarged to 18 mL (massive splenomegaly with prominent spleen vein). In flowcytometry study (antibodies acquired from BD Biosciences, San Jose, CA), there were neoplastic cells that were positive for CD19, FMC7, and co-expression of CD20/CD25, CD11C/CD22, and CD103 markers. In immunohistochemical staining, mast cells were positive for CD117 (Figure 2), plasma cells were positive for CD138 (Figure 3), and hairy cells were positive for CD20 (Figure 4).

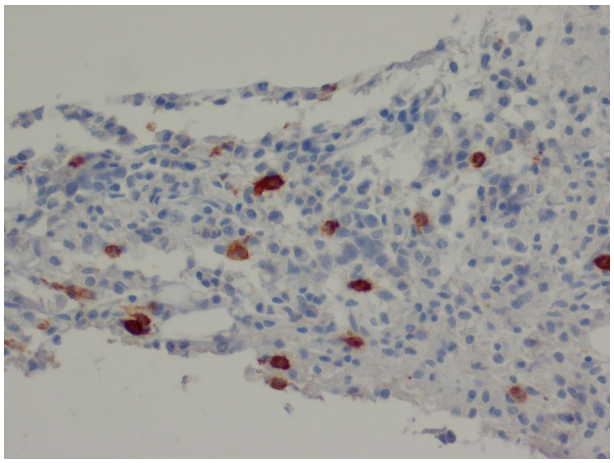

Figure 2. Immunohistochemical staining for CD117 with highlighted mast cells (×400)

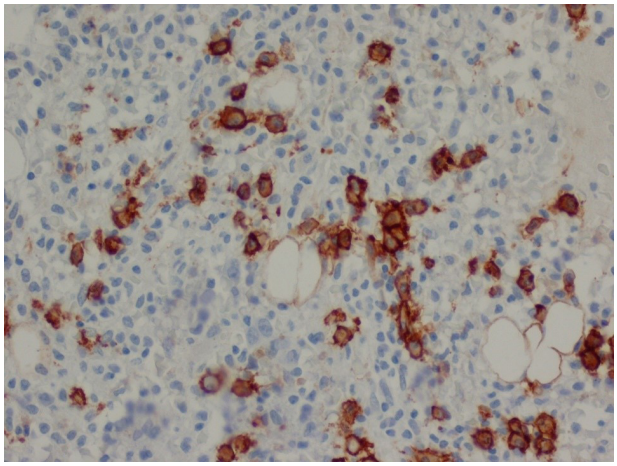

Figure 3. Plasma cells are stained with anti-CD138 (×400)

Discussion and review of the literature

HCL is an uncommon but distinct B-cell lympho-proliferative disorder affecting the blood, spleen, and bone marrow, accounting for nearly two percent of all adult leukemia cases (11,12). Its median initiation age is 50-55, with a male predominance (13,14). Although it is an uncommon malignancy, some unusual clinical presentations, such as peripheral lymphadenopathy, lytic osseous lesions, skin involvement, organ disorders, and sometimes central nervous system disease, have been noted in the literature (15-18).

Knowledge of clinical and laboratory characteristics of HCL-variant would lead to better treatment and improve the prognosis in such patients. The association of HCL with plasma cell and mast cell dysregulations is rarely mentioned in the literature. This is a malignancy or a reactive phenomenon that should be differentiated in order to determine the optimal treatment and best therapeutic and monitoring approaches in these patients (9,10). At times, plasma cell myeloma/leukemia may mimic HCL. Evidence of the co-expression of the B cell-restricted BI antigen and the plasma cell-associated PCA-l antigen in HCL, together with the observed responses of these tumor cells to known triggers of B-cell proliferation and differentiation, support the view that hairy cells may be at a late stage of B-cell ontogeny.

Rastogi et al (19) reported a case of HCL initially misdiagnosed as plasma cell dyscrasia due to odd clinical, immunophenotypic, and morphological

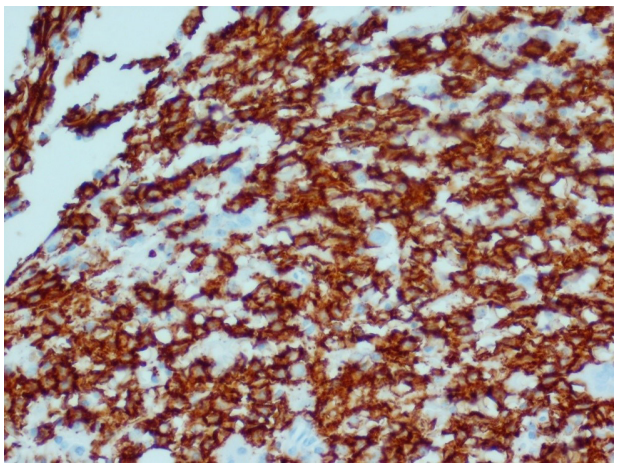

Figure 4. Immunohistochemical staining with CD20 showing tightly packed hairy cells (×400)

findings, especially the lack of CD19 and aberrant CD10 expression in the immunophenotyping study. Similar to our case, their case showed striking mast cell hyperplasia and reactive plasmacytosis.

Anderson et al (20) introduced HCL as a type of pre-plasma cell neoplasia. Such unusual morphology was also demonstrated in a case report by Sharma et al in a 60-year-old female patient (21). Also, a series of these cases were reported by Korde et al in six patients presenting the co-existence of HCL with plasma cell disorders (22).

HCL-variant is an uncommon B-cell disorder responsible for one-tenth of all HCL cases (23). The main clinical features in variant cases are splenomegaly, lymphocytosis, and cytopenias without monocytopenia (24,25). The cells in the circulating system have an intermediate morphology between pro-lymphocytes and hairy cells (26,27), as observed in our reported case. The immunophenotype showed a mature B-cell phenotype with the expression of B-cell antigens, but unlike typical hairy cells, the cells were negative for CD25 (28,29).

Rajeswari et al (30) reported a series of patients in India, predominantly female, four of whom were under the age of 40. Unlike our reported case, half of their cases had hairy cell morphology. Also, Gangadhar et al (31) reported two cases with acute onset of illness and various clinical presentations, including hairy cell morphology with a rapidly progressing acute renal failure; unlike our case, these cases were not suspected of having clinical plasma cell dyscrasia.

As an interesting point, HCL and plasma cell leukemia can each be included in the differential diagnosis of the other one (32). The diagnostic assessment of patients suspected of having plasma cell leukemia includes a review of peripheral blood smears, bone marrow biopsy and aspiration, serum protein electrophoresis with immunofixation, and protein electrophoresis test on 24-hour urine collection (32).

In comparison with gene expression profiles from the purified normal B-cell subgroups of cell populations, including germinal centers, pre-GC, and post-GC B-cells, it has been shown that the HCL cells are more related to the memory cells, suggesting a derivation from this B-cell population (33), as represented in our case study. Tanioka et al (34) reported a case of plasma cell leukemia with hairy-cell morphology and lambda-type Bence-Jones protein. However, in our study, hairy-cell morphology was not seen, and the Bence-Jones protein was not detected. The majority of atypical cells in the peripheral blood of their reported case were small lymphoid cells or plasmacytoid lymphocytes with numerous cytoplasmic hairy projections. Plasmablastic cells and tadpole-like cells were also present in their patient's bone marrow. Immunohistochemically, the atypical cells expressed the cytoplasmic lambda light chain and surface CD38 proteins but were negative for B-cell markers such as CD19, CD20, and CD79a, for which our case was also negative.

Another differential diagnosis is mast cell leukemia, which is characterized by a substantial increase in the atypical mast cells in the peripheral blood and diffuse infiltration with atypical mast cells in the bone marrow, as was seen in our patient, plus a strong association with peptic ulcer disease, prominent constitutional symptoms, and hepatosplenomegaly (35). However, among the systemic signs of this disease, only organomegaly was seen in our case. This type of leukemia usually has a very poor prognosis and short survival (36). However, another important finding in these patients is increased serum IgE levels (37), but our reported patient also had raised levels of IgA and IgG.

A distinct diagnosis of HCL-variant would result in prompt treatment in these patients accompanied by a better prognosis and higher therapeutic response. However, attention to clinical symptoms and laboratory studies, especially the immunohistochemistry and flow cytometry results in these patients, would lead to a well-documented diagnosis.

Conclusion

Various confounding factors may affect diagnoses made by hematopathologists, highlighting the importance of findings such as increased infiltration in plasma cells and mast cells. The correct diagnosis of HCL requires molecular studies and the judicious use of flow cytometry.

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Authors' Contribution

Conceptualization: Elham Jafari.
Data curation: Elham Jafari.
Formal analysis: Elham Jafari.

Investigation: Elham Jafari, Behjat Kalantari Khandani.
Methodology: Elham Jafari.
Validation: Elham Jafari, Behjat Kalantari Khandani.
Supervision: Elham Jafari.
Writing–original draft: Elham Jafari, Melika Baghershahi.
Writing–review & editing: Elham Jafari, Melika Baghershahi.

Competing Interests
The authors declare that there is no conflict of interest.

Ethical Approval
Informed consent was obtained from the patient for publication of this report.

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