Hairy cell leukemia presenting with a lytic bone lesion

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Hairy cell leukemia (HCL) is an indolent neoplasm of small mature B lymphoid cells with characteristic morphologic features usually involving the peripheral blood, bone marrow, and spleen. It constitutes approximately 2% of adult leukemias and has a male predominance. Patients usually present with weakness, splenomegaly, and pancytopenia. The overall prognosis is favorable with appropriate treatment including purine analogs, interferon-alpha, and radiation. We report a patient with a history of breast cancer who presented with a left femoral lytic bone lesion that was subsequently diagnosed as HCL by morphology, immunohistochemistry, flow cytometry, and molecular genetic techniques. It was important to biopsy the lesion to establish the correct diagnosis, as HCL is a highly treatment-responsive malignancy.

Hairy cell leukemia (HCL) is an indolent neoplasm composed of small mature B lymphocytes (1). The disease has a male predominance and generally affects the blood, bone marrow, and spleen. We report an unusual case of HCL that presented with a lytic lesion of the femur in a woman with a past history of breast carcinoma.

CASE REPORT

An 88-year-old woman with a history of breast cancer was transferred to Baylor University Medical Center at Dallas with a pathologic fracture of the left femur. Her breast cancer had been treated with chemotherapy, radiation, and surgery and had been in remission for 11 years. She presented originally to an outside hospital after suffering trauma from being hit by a scooter at a grocery store and was found to have a pathologic fracture of the left femoral neck on radiograph. On admission, her white blood cell count was 6.8 K/ μ L, hemoglobin 12.1 g/dL, and platelet count 270 K/ μ L. A monocytopenia was present, but hairy cells were not described. Further imaging showed a lytic osseous lesion of the left femoral neck (*Figure 1a*). The lesion was thought to represent metastatic breast cancer, so a fluoroscopic-guided biopsy of the left femoral neck was performed. Examination of the tissue showed small lymphoid-appearing cells with abundant clear cytoplasm and well-defined cell membranes (*Figure 1b*). Immunohistochemistry showed positivity with CD20, annexin A1, and DBA44 (B lymphocyte markers). Flow cytometry showed a 96% variable size, clonal B cell population expressing

CD10, CD11c, CD19, CD20, CD22, CD45, CD52, CD103, CD123, BCL2, and Kappa. The lesion was negative for CD5, CD11b, CD23, CD25, CD38, CD56, and FMC7. Molecular genetics was positive for the BRAF V600E mutation. These results are diagnostic for HCL. A subsequent bone marrow biopsy showed 90% involvement by HCL with a grade 2/3 reticulin fibrosis. The patient underwent orthopedic stabilization and has received a course of cladribine therapy.

DISCUSSION

HCL is an uncommon chronic B-cell lymphoid neoplasm constituting about 2% of adult leukemias. Characteristic features include pancytopenia, splenomegaly, and marrow reticulin fibrosis. The disease has distinct morphologic, immunohistochemical, flow cytometric, and molecular findings (1). HCL is characterized by expression of B-cell markers (CD19, CD20, CD22) as well as CD11c, CD25, CD103, DBA44, and annexin A1 (2). HCL has a male predominance and usually occurs in patients over 50 years old (3). With appropriate treatment, the 10-year survival exceeds 90% (1). The most frequent complications include infection, autoimmune disorders, and secondary malignancy (3). The major sites of leukemic involvement are the spleen, bone marrow, and peripheral blood (4). The diagnosis can sometimes be difficult to make, as the disease may mimic or coexist with other disorders (5). The correct diagnosis is important to establish early, as HCL has a good prognosis when appropriate treatment is given.

This case is unusual in three aspects. First, the patient did not have splenomegaly. Splenomegaly is the most common physical finding in HCL and is reported in 70% to 100% of cases (6). There is a previous case report of 4 patients with HCL without splenomegaly who also had lytic bone lesions (7). Second, the patient did not present with pancytopenia, which is common at presentation and reported in 50% to 70% of patients with HCL (1, 2). Third, HCL presenting as a lytic

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Figure 1. (a) Radiograph of the lytic lesion in the left femoral neck. (b) Hairy cell leukemia infiltrate on bone marrow biopsy (hematoxylin and eosin, 400×).

bone lesion is very unusual (2, 8). Skeletal complications can occur as a consequence of HCL, with a reported incidence of 3% and presentation about 20 months after initial diagnosis, but to present with skeletal abnormalities is very rare (9). Lytic bone lesions at presentation have been infrequently reported, with only a small number of case reports noted (6, 10). The lytic lesions usually involve the proximal femur (10). Less frequent sites include the vertebrae, pelvis, humerus, skull, and distal tibia (10). Most of these lytic lesions respond favorably to localized radiotherapy (10). The postulated mechanism by which HCL affects the bone involves tumor necrosis factor alpha, which is a growth mediator in HCL and possibly leads to bone resorption (10).

Because HCL is a treatment-responsive disease, it is important that the correct diagnosis be made in a timely fashion so proper treatment can be instituted. In this case, it was essential to obtain a biopsy even though metastatic breast disease was suspected clinically.

1. Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, Thiele J, Vardiman JW. *WHO Classification of Tumors of Haematopoietic and Lymphoid Tissues*, 4th ed. Lyon, France: IARC Press, 2008.

2. Pilichowska M, Shariftabrizi A, Mukand-Cerro I, Miller K. Primary hairy cell leukemia/lymphoma of the breast: a case report and review of the literature. *Case Rep Pathol* 2014;2014:497027.
3. Gaman AM. Hairy cell leukemia—a rare type of leukemia. A retrospective study on 39 patients. *Rom J Morphol Embryol* 2013;54(3):575–579.
4. Mirrakhimov AE, Ali AM, Barbaryan A, Anusim N, Saba R, Kwatra SG, Hussain N, Zdunek T, Gilman AD. Pancytopenia in a 70-year-old African-American male: an unusual presentation of a rare disease. *Case Rep Hematol* 2014;2014:354810.
5. Tadmor T, Polliack A. Unusual clinical manifestations, rare sites of involvement, and the association of other disorders with hairy cell leukemia. *Leuk Lymphoma* 2011;52(Suppl 2):57–61.
6. Spedini P, Tajana M, Bergonzi C. Unusual presentation of hairy cell leukemia. *Haematologica* 2000;85(5):548.
7. Venkatesan S, Purohit A, Aggarwal M, Manivannan P, Tyagi S, Mahapatra M, Pati HP, Saxena R. Unusual presentation of hairy cell leukemia: a case series of four clinically unsuspected cases. *Indian J Hematol Blood Transfus* 2014;30(Suppl 1):413–417.
8. Osman H, Roth T, Zhou J. Hairy cell lymphoma: a unique presentation of hairy cell leukaemia. *Br J Haematol* 2013;162(3):294.
9. Lembersky BC, Ratain MJ, Golomb HM. Skeletal complications in hairy cell leukemia: diagnosis and therapy. *J Clin Oncol* 1988;6(8):1280–1284.
10. Gray MT, Rutherford MN, Bonin DM, Patterson B, Lopez PG. Hairy-cell leukemia presenting as lytic bone lesions. *J Clin Oncol* 2013;31(25):e410–e412.