Not all lymphoid aggregates in chronic lymphocytic leukemia (CLL) patients are due to CLL!

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Abstract

The authors report a case of ehrlichiosis involving a bone marrow specimen from a patient with chronic lymphocytic leukemia. Since Ehrlichia may cause a lymphohistiocytic reaction in bone marrow specimens, an infectious process may be easily confused with a lymphoid neoplasm, particularly in patients with a history of lymphoid malignancy.

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***Running Head:** *Coexistence of CLL and Ehrlichia in bone marrow*

Keywords: *Ehrlichia* , ehrlichiosis, *Anaplasma,*chronic lymphocytic leukemia, tick borne illness

Key Clinical Message: Infection is a common cause of morbidity and mortality in chronic lymphocytic leukemia and should be considered when examining bone marrow specimens to identify a potentially treatable pathogen.

Conflicts of Interest: None declared

A 75-year-old man with a history of chronic lymphocytic leukemia (CLL) diagnosed in 2015 and currently treated with ibrutinib presented to the emergency department with a 1-month history of malaise and generalized fatigue. The patient denied any recent travel history and had no known sick contacts. A computed tomography scan showed hepatosplenomegaly and extensive lymphadenopathy. A complete blood count showed bicytopenia; white blood cell count, 7.8 $X10^9$/L; hemoglobin, 12.3 g/dL; platelets, 39 $X10^9$/L. Additional laboratory findings included transaminitis: AST, 81 U/L; ALT, 72 U/L; and elevated alkaline phosphatase, 353 U/L.

Given the patient's past medical history of CLL, a bone marrow biopsy was performed and showed hypercellular marrow with multiple lymphohistiocytic aggregates (1A) that mimicked CLL, but were predominately composed of T-cells rather than B-cells, highlighted by CD3 and CD20 staining (1B, 1C), favoring a reactive process. Flow cytometry demonstrated low level involvement by CLL, with approximately 3% monoclonal,

kappa-restricted B lymphocytes (1D). Review of the bone marrow aspirate showed myeloid precursors with intracellular morulae (1E) and ehrlichoisis was confirmed by detection of *Ehrlichia*species DNA by polymerase chain reaction. Morulae were not identified in the patient's peripheral blood smear; however, it has been documented that morulae can be seen in only 22% to 38% of peripheral blood smears from ehrlichoisis patients (1). Upon further discussion, the patient disclosed that he recently hiked in the woods of rural Missouri and received numerous tick bites. The patient was started on doxycycline and clinically improved.

There have been very few reports of bone marrow findings in*Ehrlichia* patients, but lymphohistiocytic aggregates have been described (2). This unique case highlights the importance of laboratory testing supported by a thorough clinical history to ensure accurate diagnosis.

Author Contributions:

LM wrote the manuscript, TW acquired data, Y-SL analyzed and interpreted data, JLF analyzed and interpretated data and wrote the manuscript.

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Figure Legend:

Figure 1: (1A) Bone marrow trephine biopsy showing lymphohistiocytic aggregate (hematoxylin and eosin, original magnification x400). Immunohistochemistry demonstrating admixed CD3**(1B)** and CD20 **(1C)** positive lymphocytes in the aggregate. **(1D)** Flow cytometric analysis of the bone marrow aspirate revealed a monoclonal B-cell population comprising ˜3% of specimen cellularity **(1E)** Review of the bone marrow aspirate revealed morulae of *Ehrlichia* organisms in granulocyte precursors.