Cytodiagnosis of Coexistence of Leukemic Infiltration and Extramedullary Hematopoiesis in a Cervical Lymph Node, in T Cell Leukemia Patient

Akanksha Bothale, Kalpana Bothale, Sadhana Mahore, Trupti Dongre
Department of Pathology, NKP Salve Institute of Medical Sciences and Research Centre, Nagpur, Maharashtra, India

Abstract

Extramedullary hematopoiesis (EMH) is a compensatory mechanism that occurs when the marrow is unable to maintain sufficient red cell mass. EMH generally occurs in the patients with deficient bone marrow hematopoiesis secondary to either peripheral red cell destruction or marrow replacement. Although EMH is known to occur in agnogenic myeloid metaplasia with myelofibrosis, chronic myelogenous leukemia, thalassemia, and infiltrative disorders, such as lymphomas, it is rare in acute leukemias. EMH is most commonly seen in the liver and spleen as a diffuse lesion. The involvement of lymph nodes in...
leukemia and EMH is known; however, to the best of our knowledge, the occurrence of both in the same lymph node has been reported in a single case report. Our case may be the second most rare case of coexistence of infiltration by leukemic lymphoblasts and EMH in the same lymph node detected on FNAC. EMH should be considered in the differential diagnosis of patients with bone marrow disorders and mass lesions in extramedullary sites.

Keywords: Extramedullary hematopoiesis (EMH), fine-needle aspiration cytology (FNAC), leukemia, leukemic infiltrate

INTRODUCTION
Extramedullary hematopoiesis (EMH) occurs when the function of bone marrow is insufficient or destroyed. Although EMH is known to occur in agnogenic myeloid metaplasia with myelofibrosis, various anemias, and chronic myelogenous leukemia, it is rare in acute leukemias. In leukemia, the infiltration of lymph nodes by leukemia cells can occur at any stage of the disease, i.e., during the course of leukemia or during relapse. Most commonly it occurs secondarily to a variety of hematological disorders such as agnogenic myeloid metaplasia, myelofibrosis, thalassemia, and infiltrative disorders such as lymphomas. The involvement of lymph nodes by leukemia and EMH is known; however, the occurrence of both in the same lymph node is reported in a single case report. After reviewing the literature, our patient appears to be the second most rare case of the coexistence of infiltration by leukemic lymphoblasts and EMH in the same lymph node.

CASE REPORT
A 14-year-old-boy reported to us with complaints of fever and weakness for 2 months. On examination, he was febrile, with ecchymotic patches all over body. Cervical lymph nodes were grossly enlarged bilaterally. They were discrete, firm and mobile, and large measuring 3 × 2 cm in size. He had facial edema with marked periorbital swelling and marked pallor. The patient had breathlessness and on chest x-ray there was mediastinal widening. On systemic examination, there was no hepatosplenomegaly.

Hematology findings
The routine hemogram showed hemoglobin level of 4.7 gm/dL, total leukocyte count of 1 lac/μL, platelet count of 60,000/μL. Peripheral smears and bone marrow aspirate smears were also studied using Giemsa stain. Peripheral blood smear examination revealed differential count-85% blasts, 5% neutrophils, 8% lymphocytes, and 2% eosinophils. Blasts were small sized with high nucleocytoplasmic ratio, 0-1 small nucleoli and agranular scanty cytoplasm [Figure 1b]. Nucleated red cells (10 per 100 WBCs) were also seen. Bone marrow aspirate smears were hypercellular with differential leukocyte count nearly similar to that of peripheral blood smear. Myeloid, erythroid and megakaryocytic series were suppressed. Cytochemical stains, such as myeloperoxidase and Sudan Black B, were done. Blast cells were negative for both stains. Acute leukemia was given as the provisional diagnosis and further evaluation was done. Then flow cytometry was done for typing of leukemia, which showed all T-lymphoid markers such as CD-3, CD-4-5, CD-7, and CD-8 positive. Myeloid and B-lymphoid markers were negative. So the diagnosis of T cell acute lymphoblastic leukemia (ALL) was offered.

Considering significant enlargement of the left cervical lymph node, FNAC was performed, using 23-gauge needle. Smears were wet fixed in alcohol for hematoxylin and eosin and Papanicolaou staining. Air-dried smears were kept for Giemsa stain.

Cytology findings
FNAC smears from lymph node showed predominantly immature large lymphoid cells, two to three times the size of small lymphocytes with scanty cytoplasm (lymphoblast) admixed with mature small lymphocytes [Figure 2a]. Also seen were small number of megakaryocytes [Figure 2b and c], occasional immature cell of myeloid series, and erythroblasts [Figure 2d]. Final diagnosis on hematological and cytological findings was given as T-cell ALL with leukemic infiltration and EMH in the cervical lymph node.

DISCUSSION
Generalized or localized lymphadenopathy preceding or developing in association with leukemia is well known, yet it is not very common.

FNA diagnosis of leukemic infiltrate in lymph node is straightforward in the patients with prior diagnosis of leukemia. In the present case, cells of other hematopoietic series, such as myeloid series cells and erythroblasts, were also present in the FNAC smears of lymph node. Thus, the large cells were recognized as megakaryocytes, as a part of extramedullary hematopoietic process.

Without the relevant hematological investigations, differential diagnosis on FNAC smears is that of non-Hodgkin’s lymphoma (NHL) and metastatic carcinoma. In a study by Kumar et al., FNA smears from lymph nodes of 14 cases of ALL were diagnosed as NHL during the initial screening. In four cases of ALL-L1, smears showed a monomorphic population of large lymphocytes (two to three times larger than RBCs) with inconspicuous cytoplasm. The nucleus occupied the entire cell and showed smooth chromatin. These cases were diagnosed as NHL, large cell, and noncleaved type. On histopathological examination also, a diagnosis of NHL was given. However, after considering the clinical history and marrow diagnosis, all of them were re-diagnosed as leukemic infiltration. Thus, clinical and hematological findings are essential for the differentiation of leukemic smears from lymphoma.
Chen et al. studied the diagnostic accuracy of FNAC in assessing extramedullary leukemic infiltration. Accurate cytologic diagnosis of extramedullary leukemic infiltration relies on detailed morphologic assessment as well as correlation with clinical examination and other relevant laboratory findings, especially in the patients whose initial symptom was a local mass.

Leukemic infiltration, which represents proliferation of primitive cells, should be distinguished from NHL. Morphologic assessment by oil immersion lens and examination of peripheral blood smears is useful in this respect.[5]

In cases of chronic myeloid leukemia (CML), rarely, the first manifestation of blast crisis is at an extramedullary site, such as the lymph node, and it is difficult to differentiate CML from malignant lymphoma on routine lymph node biopsy. Under such circumstances, FNA of the lymph node may help in rapid diagnosis because of the good morphological details of blasts and other granulocytic cells on MGG stain.[4]

EMH occurs when normal bone marrow function is insufficient or destroyed. It often involves the spleen, liver, lymph nodes, and less frequently other organs such as the kidney, retroperitoneum, and lungs.[4] On FNA, Romanowsky stains are especially helpful in the recognition of different hematopoietic cells, such as granulocytic precursors, eosinophils, and megakaryocytes. Many theories concerning the pathogenesis of these lesions have been proposed, including the extrusion of bone marrow cells consequent to marrow fibrosis/replacement by other cells. Other authors suggest reactivation of hematopoiesis in organs where it occurred in embryonic and fetal life, and increased number of circulating hematopoietic stem cells which embolize to different organs.[6]

Megakaryocytes can resemble multinucleated RS cells as they can have a large, bilobed, or multilobated nucleus with abundant, pale, and fragile cytoplasm. However, the smears in Hodgkin’s disease reveal a background of lymphocytes, plasma cells, histiocytes, and eosinophils and the RS cells have huge prominent nucleoli.[7]

EMH is usually a microscopic finding. However, it may present as a mass-forming lesion making it amenable to fine-needle aspiration biopsy (FNAB). When mass-forming EMH occurs, it can simulate a neoplasm clinically and radiologically. Additionally, the megakaryocytes can mimic malignant neoplastic cells, particularly if EMH is not a considered diagnosis.[8]

This was a rare case diagnosed on FNAC as infiltration of lymph node by leukemic cells along with features of EMH. Recognition of the different cells was possible with Romanowsky staining on FNAC smears. EMH should be considered in the differential diagnosis of the patients with bone marrow disorders and mass forming lesion in extramedullary sites.

**Declaration of patient consent**
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/ their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**
There are no conflicts of interest.

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