



An unusual case report of endobronchial deposits of chronic lymphocytic leukemia: Diagnosed on cytology with histopathology correlation

Authors

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Abstract

Chronic lymphocytic leukemia (CLL) is the most common B-cell leukemia seen in adults in the world. Respiratory tract illnesses are common in patients with CLL and result in significant morbidity and mortality. Patients with leukemic bronchopulmonary involvement (LBPI) often present with vague symptoms like dry cough, progressive dyspnoea, chest pain and hemoptysis and diagnosis becomes challenging in such patients. Pulmonary involvement in patients may occur in various forms. The diagnosis often becomes challenging and requires combination of tests including computed tomography imaging, blood work up, and bronchoscopy or lung biopsy to rule out infectious etiologies. We present a case of leukemic bronchopulmonary involvement diagnosed on cytology leading to the diagnosis of CLL.

Keywords: *Chronic lymphoproliferative disorder (CLL), endobronchial biopsy, leukemic bronchopulmonary involvement (LBPI).*

Introduction

Chronic lymphocytic leukemia /small lymphocytic lymphoma (SLL) is a clonal lymphoproliferative disorder characterized by proliferation of morphologically and immunophenotypically mature lymphocytes. CLL/SLL usually proceed through different phases: an early phase in which tumor cells are small in size, with a low proliferation rate, and a transformation phase with frequent occurrence of extramedullary proliferation and an increase in large, immature cells.^[2] Pulmonary involvement in CLL can occur in different forms. Diagnosis is challenging in most cases, therefore BAL, endobronchial and transbronchial biopsies becomes useful in diagnosis.^[3]

Case report

A 70 year old male patient presented with dyspnoea from one month and weightloss over 2 years. On CT chest small enhancing soft tissue lesions seen in posterior segment of B/L upper lobes with significant heterogeneously enhancing mediastinal and B/L hilar lymphadenopathy. Bronchoscopy was done which revealed 1-2 nodules in right main bronchus (mid portion) and multiple nodular infiltrations in left main bronchus (lower part) extending upto left lower lobe airway. Endobronchial brushings and biopsy were taken and sent for cytology and histopathology examination respectively. Endobronchial brushings showed scant cellular smears which was inadequate for any definite opinion. USG guided FNAC was also done from prepancreatic lymph node which revealed features suggestive of lymphoproliferative disorder (FIG-

1A & B). Endobronchial bronchial biopsy showed sheets of small mature lymphocytes with clumped chromatin, inconspicuous nucleoli with scant cytoplasm and occasional mitotic activity (FIG-2A & B) and diagnosis of lymphoproliferative disorder was given. Bone marrow biopsy and aspiration was further done with flow cytometry. Bone marrow aspiration showed 61% lymphocytes which were predominantly small sized and show clumped chromatin and scant

cytoplasm with few lymphoid cells were small to medium sized with relatively clumped chromatin and conspicuous nucleoli and bone marrow biopsy showed histopathological features of chronic lymphocytic leukemia (FIG-3). IHC was done to confirm the diagnosis of lymphoproliferative disorder which showed positivity for CD 20, CD 5, CD19, CD23 (FIG-4A&B) and negative stain for CD15 and thus the final diagnosis of chronic lymphoproliferative disorder was given.

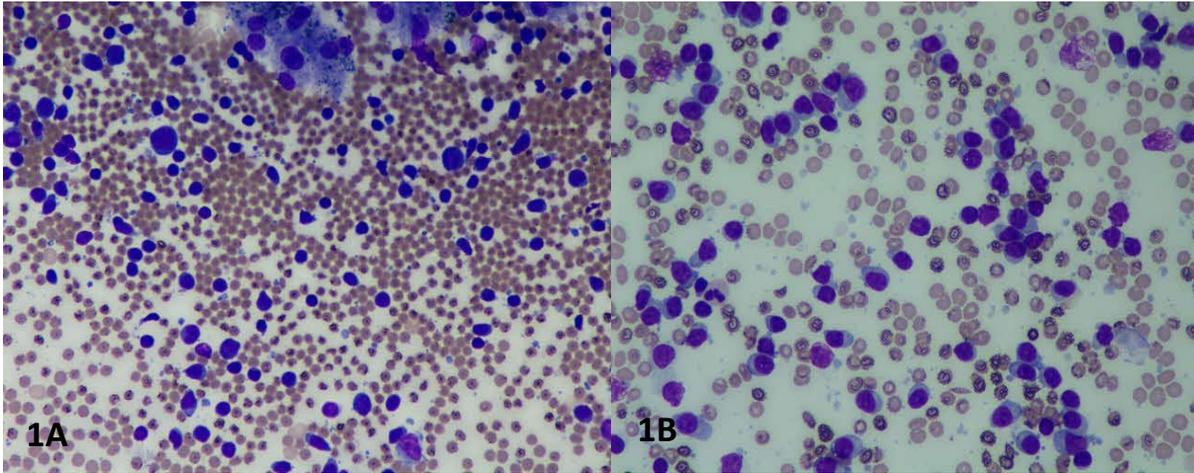


Figure 1A: Photomicrograph of FNA smears from peripancreatic lymph node showing small to intermediate sized lymphoid cells infiltration in the lymph node (Giemsa stain;100x)

Figure 1B: Photomicrograph of FNA smears from peripancreatic lymph node showing infiltration of chronic lymphocytic leukemia in the lymph node. (Giemsa stain;400x)

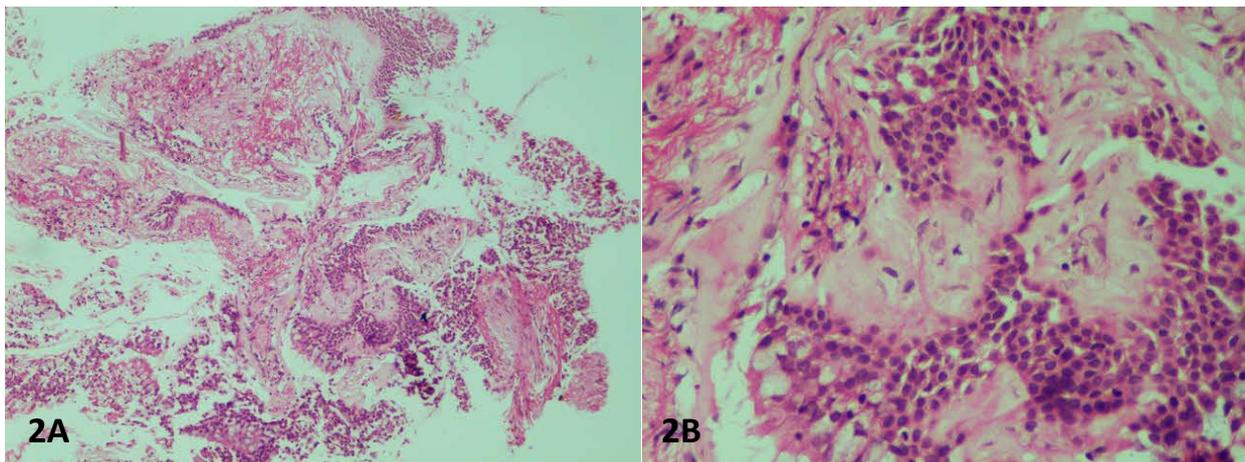


Figure 2A: Photomicrograph of endobronchial biopsy fragments revealing sheets of small to intermediate sized lymphoid cells in the stroma (H&E; 100x)

Figure 2B: Photomicrograph of endobronchial biopsy fragments revealing sheets of lymphoid cells of chronic lymphocytic leukemia in the stroma (H&E;400X)

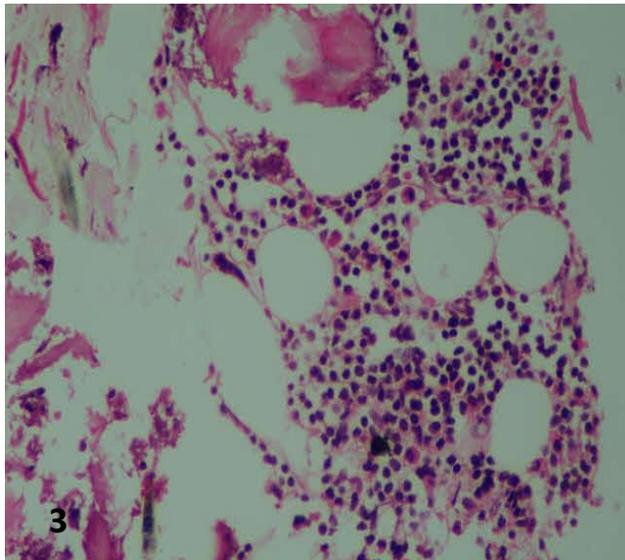


Figure 3: Photomicrograph of bone marrow biopsy showing bony trabeculae with clusters of lymphoid cells admixed with other hematopoietic lineage elements (H&E; 400X)

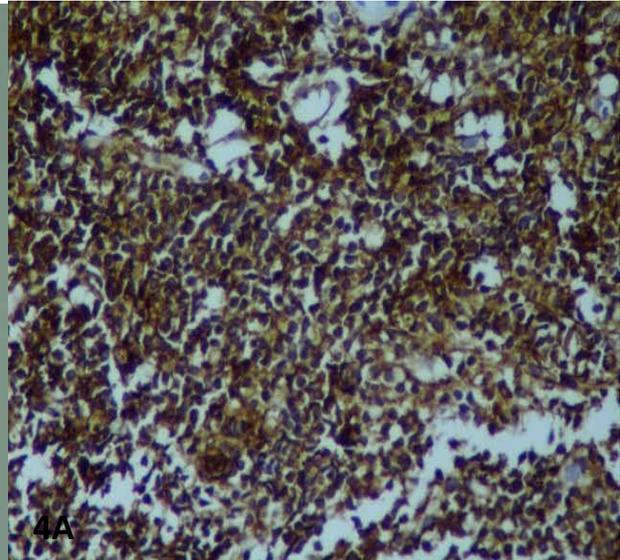


Figure 4A: Photomicrograph of CD20 immunostained endobronchial biopsy showing membranous positivity in the lymphoid cells (IHC;400X)

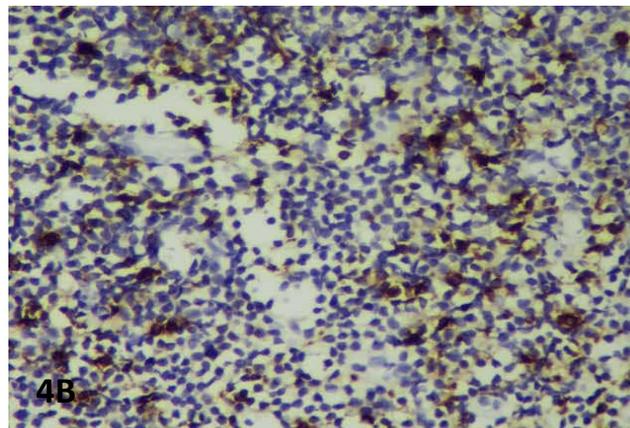


Figure 4B: Photomicrograph of CD5 immunostained endobronchial biopsy showing membranous positivity in the lymphoid cells (IHC; 400x)

Discussion

Chronic lymphocytic leukemia (CLL) is the most common adult leukemia in western countries, accounting for approximately 30% of all leukemias. It is a B-cell disorder that mainly affects older adults, with a median age at diagnosis of 70 years.^[1] Respiratory tract illnesses are common in patients with CLL and result in significant morbidity and mortality.

Thoracic complications of CLL can be classified into three groups: 1) infectious complications, which are the most frequent and are directly related to the severity of immunodeficiency secondary either to leukemia or therapy; 2) pleural

effusions are either in CLL localisation or related to venous or lymphatic compression caused by a mass or lymph node, and 3) specific bronchopulmonary involvement which is usually secondary to lymphocytic infiltration. Specific bronchopulmonary involvement due to chronic lymphocytic leukemia or pathological leukemic bronchopulmonary infiltration (LBPI) is rare.^[4] Infiltration of the lung parenchyma with leukemic cells may be common and autopsy studies report LBPI in 24% to 64% of the patients dying with acute leukemia.^[5] However, LBPI due to CLL are rarely reported in the literature.^[6]

Patients with LBPI often present with vague symptoms like dry cough, progressive dyspnoea, chest pain and hemoptysis and diagnosis becomes challenging in such patients.

When LBPI is identified along with findings of inflammation at extra nodal sites like the lung, it is often uncertain as to whether the CLL cells represent truly pathologic involvement (a pathologic infiltrate) or whether the CLL cells are recruited nonspecifically as a result of ongoing inflammation and host response (a “passenger effect”). LBPI often occurs along pulmonary lymphatic drainage and around vessels and the bronchopulmonary axis. However, the location of pulmonary infiltrate is varied and may also be diffuse and subpleural.^[6]

Infection is the most common cause of pulmonary infiltrates in patients with CLL; however, direct infiltration by leukemic cells may cause signs and symptoms indistinguishable from infection. In such cases, a biopsy is necessary to establish a definitive diagnosis, and physicians should be aware of the clinical picture to render an informative diagnosis.^[7]

Thus, the diagnosis of LBPI is based on a combination of tests including computed tomography imaging, blood work up, and bronchoscopy or lung biopsy to rule out infectious etiologies.^[4]

Pure leukemic infiltrates show a monotonous/monomorphic population of atypical lymphoid cells scattered diffusely or forming aggregates.^[6] Immunohistochemical stains which can be used to differentiate lymphoma subtypes includes CD5, CD3, CD20, CD79a, PAX5, CD23, BCL2, BCL6, Ki67, cyclin D1, FMC7, CD43, CD38, and CD10.^[8]

Other ancillary studies like flow cytometry, cytogenetics, and molecular studies aids in determining clonality, as well as subtyping. CT of the chest, abdomen, and pelvis is not routinely performed as part of the pretreatment evaluation. However, a CT scan should be done in any patient in whom enlarged abdominal or pelvic nodes are suspected based on any evidence of

complications.^[9] Conversely, a reactive process can be diffuse or localized. It consists of a mixture of lymphocytes, neutrophils, eosinophils, and histiocytes in varied proportion. Neutrophils predominate in an acute process, whereas chronic inflammation shows more lymphocytes and macrophages. Necrosis can be seen in both acute and chronic inflammation.^[10] Necrosis is less commonly seen in lymphomas. A mixture of both B and T-lymphocytes, positive for B and T-cell markers, respectively, by immunohistochemistry, are seen in reactive processes also. The cells in lymphoproliferative disorders may show either B or T-cell clonality.^[8]

Conclusion

Early diagnosis of LBPI enables physicians to discontinue antibiotic therapy and promptly initiate CLL-directed therapy. Further studies are needed to determine the cause of leukemic infiltration of the lung. In our case diagnosis was suggested on FNAC lymph node and was confirmed by lung histopathologic correlation and bone marrow examination.

References

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