



## A rare case of acute lymphoblastic leukemia/lymphoma with spill over in inguinal lymph node in a middle aged patient

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### Introduction

Acute lymphoblastic leukemia (ALL) is a cancer of lymphoid blood cells characterized by large numbers of immature lymphocytes. ALL progresses rapidly and is fatal if left untreated.<sup>(1)</sup> Precursor lymphoid neoplasms are categorized as B and T lymphoblastic leukemia/lymphoma.<sup>(2)</sup> Leukemia and lymphoma are overlapping clinical presentations of the same disease (i.e, B-ALL/LBL); diagnosis and classification do not distinguish between these entities. B-cell acute lymphoproliferative disease manifest as pure leukemia (B-ALL) in 80% cases, isolated extra medullary disease (B-LBL) in 10% and mixed B-ALL/B-LBL in 10% cases.<sup>(3)</sup> B-ALL/B-LBL is rare in adults and cases with spill-over in inguinal lymph nodes has not been reported as per our knowledge.

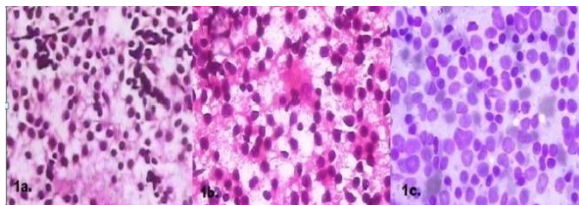
### Case History

A 52 year old male reported with the chief complaints of pain abdomen, dyspepsia, pain in shoulder and generalized weakness for 5 months. On physical examination, patient had pallor and enlarged bilateral inguinal lymph nodes. On systemic examination patient had enlarged liver

and spleen rest of the systems were within normal limits. Ultrasonography revealed hepatosplenomegaly.

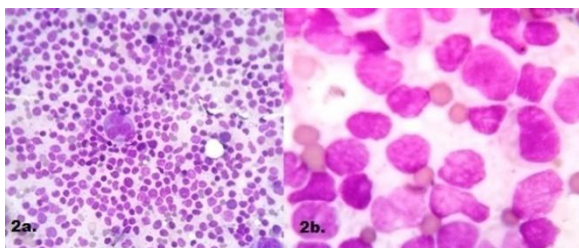
In hematological investigations, patient's total leucocyte count was normal with low platelet count of 32000/cumm. Peripheral smear showed RBCs with moderate anisopoikilocytosis with evidence of 0-1 nucleated RBCs/100 WBCs. Atypical lymphocytes of blastoid morphology were seen. Rests of the hematological and routine serological investigations, urine routine and microscopic examination were within normal limits. Chest X-Ray was normal.

Fine needle aspiration (FNA) from inguinal lymph node was performed. Smears were prepared and stained by MGG and H:E technique. On microscopic examination, smears were cellular consisting of predominantly medium to large lymphoid cells with enlarged nuclei and scanty, finely granular and basophilic cytoplasm admixed with few mature lymphocytes (Figure.1a,b,c) altogether suggestive of leukemia/lymphoma.



**Figure 1 (a,b,c).** Fine needle aspiration cytology showing atypical medium to large lymphoid cells (H&E. & M.G.G.10x &40x).

As patient had severe anemia, a bone marrow aspiration was done which revealed a cellular marrow with myeloid, erythroid and megakaryocytic lineage markedly suppressed and replaced by proliferating moderate to large size blast cells comprising 90% of bone marrow cell population. Blast cells had pleomorphic nuclei with 1-2 nucleoli, clumped chromatin, irregular nuclear membrane and scanty to moderate amount of basophilic cytoplasm (Figure. 2a, b). The impression of bone marrow aspiration examination was ALL.



**Figure 2(a,b).** Bone marrow aspiration showing proliferating moderate to large size lymphoblasts (MGG 40x&100x).

The patient’s blood sample was taken for flow cytometric examination and the results were as follows:

**Cell preparation method:** Stain-Lyze-Wash

**Population gated:** Blasts

**Gated cells (% of all cells):** CD45/SSC gating shows 8.5% blast with negative to dim CD45 and low side scatter which exhibit immunophenotype as shown in Table 1.

**Interpretation:** The immunophenotypic analysis of gated population of blast (8.5%) suggests B-Lymphoid cell (Precursor B cell) immunophenotype with aberrant expression of CD 13.

B-cell ALL translocation panel was applied on patient’s blood sample by Multiplex PCR & gel electrophoresis technique. The hybrid transcripts for BCR/ABL-1, ETV6/RUNX1, E2A/PBX1 and

MLL/AF4 were not detected in the leukocytes of the sample.

**Table 1.**

Markers	Percentage Positivity	Remarks
<b>Non lineage specific</b>		
CD 34	69.4	Positive, Moderate
Tdt	27.0	Positive, DIM
HLA -DR	<b>75.5</b>	Positive, Moderate
<b>Lymphoid T Cell</b>		
CD 3	3.7	Negative
CD 4	14.1	Negative
CD 5	0.5	Negative
CD 7	2.4	Negative
CD 8	4.8	Negative
cCD 3	2.7	Negative
<b>Lymphoid B Cell</b>		
CD 10	77.8	Positive, Moderate To Bright
CD 19	68.0	Positive, Moderate
CD 20	5.9	Negative
cCD79a	20.5	Positive, Dim
CD 13	49.5	Positive, Dim
CD 33	0.3	Negative
CD 117	0.5	Negative
cMPO	8.6	Negative
CD 11c	2.4	Negative

**Discussion**

ALL is a clonal hematologic disorder. It involves excessive proliferation and impaired differentiation of leukemic blasts that lead to inadequate normal hematopoiesis. Thus, patients usually present with symptoms resulting from bone marrow failure. The extra-medullary form of this disease is rarely reported. However, when found, it most commonly involves the bones, followed by soft tissue, skin and lymph nodes.<sup>(4)</sup>

The WHO classification of tumors of hematopoietic and lymphoid tissues divides B-cell malignancies into precursor B-cell neoplasms and mature B-cell neoplasms. While the rate of remission is high in both adults and children, the 5 year survival rate is much lower in adults.<sup>(2)</sup> B-ALL/LBL accounts for 2% of lymphoid neoplasms diagnosed in the United States.<sup>(3)</sup> Adulthood ALL is a rare disease. In contrast to childhood ALL, survival for adults with ALL is poor.<sup>(5)</sup> In the present case the patient was a middle aged man.

On physical examination, peripheral lymph node involvement is seen in 60-80% of patients. <sup>(6)</sup> Hepatosplenomegaly is a common finding in patients of ALL and causes abdominal discomfort as seen in our patient.

Baljevic et al stated ALL patients demonstrate anemia and thrombocytopenia to varying degrees. WBC counts at initial presentation can vary significantly, circulating lymphoblast cells are seen on peripheral blood smears in the majority of cases. <sup>(7)</sup> Similar findings were noted in our case.

In leukemia, infiltration of lymph nodes by leukemia cells can occur at any stage of the disease, i.e. during the course of leukemia, prior to onset of marrow leukemia or during relapse. Singhal *et al* reported a similar case with FNA findings of predominantly immature lymphoid cells conforming to morphology of lymphoblasts with few mature lymphocytes and numerous lymphoglandular bodies in the background as seen in our case. <sup>(8)</sup> Accurate cytologic diagnosis of extramedullary leukemic infiltration relies on detailed morphologic assessment, clinical examination and relevant laboratory findings. <sup>(8)</sup>

Bone marrow aspiration and biopsy are the definitive diagnostic tests to confirm the diagnosis of leukemia. The diagnosis of ALL is made when at least 30% lymphoblasts (FAB classification) or 20% lymphoblasts (WHO classification) are present. <sup>(9)</sup> In our case BMA revealed more than 90% blasts.

The most common rearrangement in B-ALL is the t(12;21) (p13;q22) rearrangement that encodes *ETV6-RUNX1* followed by *MLL* rearrangements t(4;11)(q21;q23) */MLL-AFF1(AF4)*, *BCR-ABL1* t(9;22)(q34;q11) and E2A-PBX1 t(1;19) (q23;p13). <sup>(10)</sup> But these translocations were not detected in our patient.

In B-lineage ALL the most important markers for diagnosis are CD19, CD20, CD22, CD24, and CD79a, the earliest being CD19, CD22 and CD79a. <sup>(11)</sup> A positive reaction for any two of these three markers, identifies pro-B ALL. <sup>(12)</sup> In our case, tumor cells were positive for CD34, HLA-

DR, TdT, CD10, CD19, CD79a and CD13 with aberrant expression of CD13.

Our case of precursor B-ALL with spill-over in inguinal lymph node is a rare finding in a middle aged patient. This case further illustrates the need for comprehensive immunophenotyping and genetic testing when establishing an accurate diagnosis of ALL, as this could impact management and will further add to the current knowledge. Prognosis is poor in adults due to high-risk disease characteristics and significant toxicity associated with chemotherapy in adults.

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