A case of Acute Lymphoblastic Leukemia with rare t(11;22)(q23;q13)

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Clinics

Age and sex
14 months old male patient.

Previous history
No preleukemia, no previous malignancy, inborn condition of note. Patient has hemoglobin S trait.

Organomegaly
Hepatomegaly, splenomegaly, enlarged lymph nodes, central nervous system involvement.

Blood

WBC : 33 X 10^9/l
HB : 2.6g/dl
Platelets : 1 X 10^9/l
Blasts : 72%
Bone marrow : 100 bone marrow blast replacement.

Cyto-Pathology Classification

Cytology
Acute lymphoblastic leukemia (ALL) with L1 morphology

Immunophenotype
Flow cytometry of bone marrow aspirate identified a dim CD45 lymphoblast population (85%) expressing HLA-DR, CD19 and partially expressing CD10, CD22, CD9 and CD40.

Rearranged Ig Tcr
Not performed.

Pathology
Bone marrow aspirate appeared hypocellular with 95% lymphoblasts of L1 morphology, 2% myeloid series, and 3% erythroid series.

Electron microscopy
Not performed.

Diagnosis
CD34 negative B-precursor ALL.

Survival

Date of diagnosis: 01-2011
Treatment: Methotrexate, Cytarabine, Vincristine, Dexamethasone, PEG-asparagase
Complete remission : no
Treatment related death : no
Relapse : no
Status: Alive. Last follow up: 10-2011
Survival: 9 months

Karyotype

Sample: Bone marrow aspirate
Culture time: 24hr without stimulant and 48hr with 10% conditioned medium.

Banding: GTG

Results
46,XY,der(X)t(X;9)(p11.1;q11),add(9)(q11),t(11;22)(q23;q13)[20] (see Figure 1). Post induction bone marrow study demonstrated a normal 46,XY karyotype.
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Figure 1: G-banded karyotype showing 46,Y,der(X)t(X;9)(p11.1;q11),add(9)(q11),t(11;22)(q23;q13). Arrows pointed to t(11;22).

Figure 2: FISH. A. Interphase hybridized with LSI MLL dual-color break apart probe showed a split signal pattern of MLL (1O1G1F). B. Metaphase hybridized with BCR/ABL dual-fusion probe showed 2O2G signaling. C. For identification of chromosome 22, the same metaphase subsequently hybridized with LSI MLL probe showing relocation of the telomeric side (orange signal) of MLL to 22q confirming t(11;22)(q23;q13) (arrows). Note: G= green; O= orange; F= fusion.

Other Molecular Studies

Technics:
Fluorescence in situ hybridization (FISH) using the ALL panel DNA probes including CEP 4, 10, and 17 alpha satellite probes, LSI MLL dual-color break apart probe, BCR/ABL and TEL/AML1 dual-fusion translocation probes was performed (Abbott Molecular, Downers Grove, IL).

Results:
Hybridization with MLL probe produced a split/translocation pattern in 61% of interphase cells. Metaphase FISH showed that the telomeric region of MLL gene was translocated to 22q13 distal to BCR (Figure 2). The hybridization with the BCR/ABL probe showed two signals each (unfused), however on a previously G-banded metaphase it appeared that the BCR signals remained on chromosome 22 while one ABL signal was translocated to der(X). The remaining probes produced a normal hybridization pattern.

Comments
The patient described here is a 14 month-old-male presented with an upper respiratory tract infection unresponsive to antibiotics. Subsequently he was diagnosed with high risk B-precursor ALL due to the positivity of MLL/11q23 rearrangement. The patient
was started on a Children's Oncology Group induction chemotherapy protocol. Secondary to his high risk status, the patient is being evaluated for a bone marrow transplant. At time of diagnosis chromosome analysis revealed the presence t(11;22)(q23;q13) in all 20 metaphases and rearrangement of the MLL gene.

Translocations involving the MLL/11q23 region are the most common genomic aberrations in infant ALL seen in ~80% of cases (Raimondi, 2004). Generally leukemia harboring MLL translocation is clinically aggressive and associated with poor prognosis. The most common chromosomes involved in 11q23 translocations are t(4;11) followed by t(11;19) and t(9;11). Additionally, leukemia with MLL/11q23 translocations are frequently associated with over expression of FLT3, therefore, targeted therapy inhibitors of FLT3 (a tyrosine kinase) may be beneficial for those patients. Currently there are only three reported cases in the literature with t(11;22)(q23;q13), unlike our case all having secondary acute myeloid leukemia with prior therapy of topoisomerase II inhibitor (table 1). Moreover, rearrangement of the MLL gene and MLL-EP300 fusion gene were demonstrated in those three cases (Ida et al., 1997; Ohnishi et al., 2008; Duhoux et al., 2011).

The clinical presentation of our case is quit different from these three cases. Although our case had a rearrangement of the MLL/11q23 gene, the MLL-EP300 fusion gene was not tested. Because the partner genes involved in MLL/11q23 translocations are markedly heterogeneous, it remains unclear whether EP300 or other gene is involved in the present case which may be responsible for the different phenotype of this leukemia.

### Table 1: AML cases with t(11;22)(q23;q13) reported in literature.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Primary Malignancy</th>
<th>Leukemia</th>
<th>Karyotype</th>
<th>Gene</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 Y/M [2]</td>
<td>Non-Hodgkin Lymphoma</td>
<td>AML M1</td>
<td>48,XY,+8,+8,t(11;22)(q23;q13)</td>
<td>MLL-EP300</td>
</tr>
<tr>
<td>5 Y/F [3]</td>
<td>Neuroblastoma</td>
<td>AML M2</td>
<td>46,XX,t(1;22;11)(q44;q13;q23),t(10;17)(q22;q21)</td>
<td>MLL-EP300</td>
</tr>
</tbody>
</table>

### References


This article should be referenced as such: