

T-cell Acute Lymphoblastic Leukemia with del (7) (q11.2q22) and Aberrant Expression of Myeloid Markers

Ahmad Ahmadzadeh¹, Sajedeh Saedi², Kaveh Jaseb^{2*}, Ali Amin Asnafi², Arash Alghasi², Najmaldin Saki²

¹Cancer, Petroleum and Environmental Pollutants Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

²Research Center of Thalassemia & Hemoglobinopathy, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Corresponding author: Kaveh Jaseb M.D

Research Center of Thalassemia & Hemoglobinopathy, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Email: k_jaseb@yahoo.com

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ABSTRACT

T cell acute lymphoblastic leukemia (ALL) is an invasive disease with a higher incidence in children and adolescents. In terms of Immunophenotype, T-ALL is positive for CD2, CD7, CD34 and HLA-DR, and the level of these markers is increased with increasing age. In addition, the myeloid markers (CD13, CD33) are sometimes expressed in T-ALL. In this study, we introduce a rare case of a 28-year-old woman with T-ALL with aberrant expression of myeloid markers (CD13), without lymphadenopathy and with 94% blasts in bone marrow specimens. The patient has the rare karyotype of 46,XX del(7)(q11.2q22). The presence of del7 is a rare phenomenon in T-ALL.

KEY WORDS: Acute lymphoblastic leukemia, Myeloid, T cell

INTRODUCTION

Acute lymphoblastic leukemia (ALL) is the most common malignancy in children. There are two subtypes of ALL: 1-Acute lymphoblastic leukemia of T cells 2-Acute lymphoblastic leukemia of B cells.^{1, 2} T-ALL is an aggressive cancer, which mainly occurs in children and adolescents. T-ALL is more common in men than women, with a prevalence of 10-15% in children and 25% in adults.^{3, 4} T-ALL occurs due to acquired chromosomal translocations and other genetic and epigenetic abnormalities in T lymphoblasts, leading to aberrant expression of specific transcription factors such as: HOX11, TAL1/SCL and LYL1 oncogenic transcription factors.⁵ Characteristic features of T-ALL include a large number of blasts in peripheral blood and bone marrow, enlarged lymph nodes in mediastinum and frequent involvement of central nervous system.⁷ Although the outcome of disease has improved

using current treatments but, five-year survival rate is 50-60%.⁸ Immunophenotyping of ALL shows positive TdT in pre T ALL and likely expression of CD10, CD79a and cCD3 markers. Although myeloid markers (CD13-CD33) may be expressed, expression of CD117 is a rare phenomenon.¹ In one study, CD7 expression has been indicated in all cases of T-ALL, while the level of CD2 is decreased with increasing age, and HLA-DR and CD34 level is increased with age.⁹ Molecular analysis of common genetic changes in leukemia cells leads to better understanding of the pathogenesis and prognosis of ALL, although the prevalence of genetic changes is different in children and adults.¹⁰ More than 50% of T-ALL cases show mutations in NOTCH1 gene, an important regulator of growth in normal T cells.¹¹

We describe a case of T-ALL with aberrant expression of myeloid antigens along with the rare karyotype of del7 (q11) in a young woman.

Complete loss of chromosome 7 (-7) or deletion in q arm of this chromosomes is common in malignant myeloid disorders (AML and MDS), and del(7)(q11.2q22) has been rarely reported in T-ALL.¹²⁻¹⁴ We discuss the expression of this cytogenetic abnormality along with laboratory findings and prognosis of the disease.

The Patient's History

A 28-year-old woman with severe lethargy visited Shafa Hospital in Ahwaz. After performing CBC, high leukocytosis (WBC=19.11×10⁹/L), anemia (RBC=1.45×10¹²) and thrombocytopenia (PLT=5×10⁹/L) was diagnosed (other hematologic indices are given in Table 1).

Table 1. CBC Results upon Admission of the Patient Indicating Severe Anemia, Thrombocytopenia and Leukocytosis in the Patient

| | |
|------|--------------------------|
| WBC | 19.11×10 ⁹ /L |
| Neu% | 5.4 |
| Lym% | 69.6 |
| Mon% | 24.7 |
| Eos% | 0.1 |
| Bas% | 0.2 |
| RBC | 1.45×10 ¹² |
| HGB | 4.1g/dl |
| HCT | 12.7% |
| MCV | 87.6 Fl |
| MCH | 28.3 Pg |
| MCHC | 32.3 g/Dl |
| PLT | 5×10 ⁹ /L |

Abbreviation: Neu(Neutrophil); Lym(Lymphocyte), Mon(Monocyte), Eos(Eosinophil), Bas(Basophil)

The patient had no significant medical history except postpartum anemia. No abnormality was detected in ultrasound examination of the abdomen and pelvis, and lymph node enlargement was not seen in patient's radiography. Biochemical and serologic examination showed high LDH (583 IU/L) level, negative direct and indirect Coomb's test and very high ferritin levels (900.9 ng/ml). 94% blasts in the bone marrow smear was estimated (Figure 1), and myeloperoxidase staining (MPO) was negative in these blasts. Flow cytometry indicated the expression of CD34 (60%), CD117 (17%), HLA-DR (82%), CyCD3 (85%), CD7 (85%), CD2 (89%), CD13 (59%) and CD33 (5%) markers by blasts, and other markers were negative in them. In cytogenetic

examination of the patient, 46,XX del(7)(q11.2q22) was detected (Figure 2).

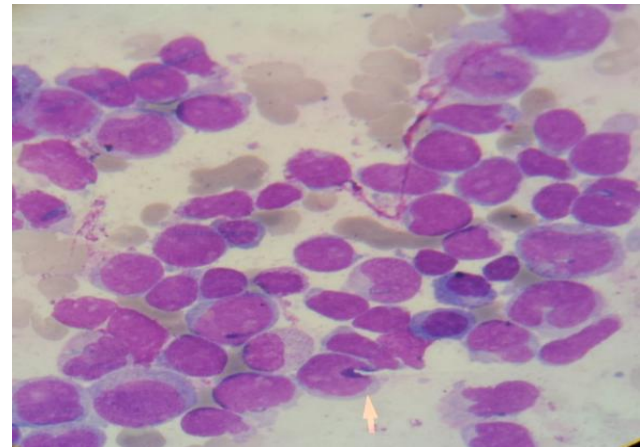


Figure 1. blasts in the bone marrow smear

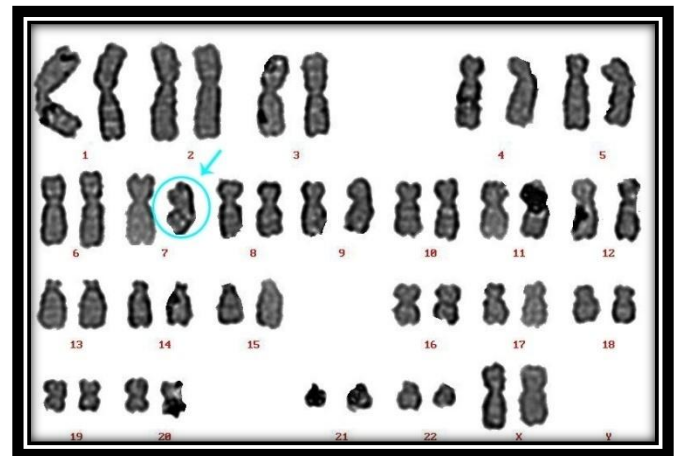


Figure 2. analysis of patient's karyotype using GTG banding indicating rare chromosomal aberration of del(7)(q11.2q22)

Simultaneous expression of myeloid and lymphoid markers on blasts along with presence of del(7)(q11.2q22) specific for acute myeloid leukemia (which is rarely reported in T-ALL) complicated the diagnosis. At first, two-phenotype acute leukemia was suspected, but it was ruled out in further investigation as the most common myeloid markers in acute two-phenotype leukemia are CD33, CD13, CD15 (CD19, CD79a, CD22 for B lymphocytes and CYCD3, CD7, CD2 for T lymphocytes), but in this patient myeloid and B lymphocyte markers were not expressed or had a low level of expression. Considering high expression of T lymphocyte markers and positive PAS staining

in the blasts, final diagnosis was T-ALL with aberrant expression of CD13 and del(7)(q11.2q22).¹⁵ The patient underwent chemotherapy with treatment protocol of endoxane, doxorubicin, prednisone and vincristine for ALL. Flow cytometry was performed one month later (1/2013), and non-conclusive bone marrow with erythroid hyperplasia was diagnosed. Response to treatment was good, but the patient became BM transplant candidate because of high risk. After finding an individual with similar HLA, the patient underwent BM transplantation, and is currently in remission (3/2013).

DISCUSSION

T-ALL is an aggressive cancer causing 10-15% of ALL cases in children and 25% in adults. Aberrant phenotype (MY+ALL) has been reported in 10-47% of ALL cases.^{4, 16} CD33 myeloid antigen has been detected in 39% of adult B-ALL cases and 33% of T-ALL cases. Common myeloid antigens in ALL are shown in Table 2. ALL cases expressing CD13 and CD33 myeloid antigens are associated with a favorable outcome in adults, with a poor outcome in B-ALL but not in T-ALL.¹⁷ In another study on ALL, approximately 20% of the patients showed simultaneous expression of T and myeloid antigens, and no difference in response or survival was observed between patients with or without myeloid antigen who expressed T antigens.¹⁸ In this paper, we have studied an ALL patient with aberrant expression of myeloid antigens and rare karyotype of del(7)(q11.2q22). Heerema et al., in their study concluded that the survival rate was not different in adult ALL patients with or without deletion of chromosomes 5 and 7 but the disease outcome was unfavorable. Monosomy 7 and del(7q) are associated with poor outcome in AML. del(7p) in ALL in children is associated with poor outcome but deletion of 7q is not. Deletion in chromosome 7 and monosomy of 7 has been reported in adult ALL, and there are reports of deletion in 7q11.2 and 7q11 in ALL.¹² In 1977, a case of ALL with Philadelphia chromosome and abnormalities of chromosome 7 [monosomy 7 in 60% of blasts and del (7q11) in a small percentage of the cells] was reported.¹³ Abnormalities of chromosome 7 are associated with impaired granulocyte movement, susceptibility to infection, rapid disease progression and poor

response to treatment.¹⁹ In this case, we did not detect any infection and the patient's response to treatment was good. 7/del (7q) occurs in three cases: 1- in patients with spontaneous MDS/AML, 2- in treatment dependent MDS/AML or occupational/environmental exposure to mutagens, 3-leukemia arising from individual susceptibility to AML, Fanconi's anemia, congenital neutropenia and NF1 commonly detected with -7/del (7q).¹⁴ Loss of chromosome 7 or deletion in long arm of this chromosome is common in MDS in children and adults, and is in fact the most common cytogenetic abnormality in children MDS, detected in 30% of the cases.^{20, 21} The long arm of chromosome 7 contains some tumor suppressor genes, and these genes are probably located on loci usually deleted in patients with del7.²² Important regions of chromosome 7 include 7q22 and 7q32-33.²³

CONCLUSION

Deletion detection in various regions of chromosome 7 in T and even B acute lymphoblastic leukemia demonstrates the applicability of deletions in this chromosome for disease diagnosis and prognosis. T-ALL with aberrant expression of myeloid antigens is not different from T-ALL without the expression of myeloid antigens in view of outcome.¹⁸ According to good response of our patient to therapy, deletion in q11 region of chromosome 7 is likely to be associated with a favorable prognosis and response to therapy; however, based on previous findings, del7 is associated with poor response to treatment. Table 3 shows deletions in different regions of chromosome 7 in various types of leukemia.

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Table 2. Specific CD Markers of ALL Subtypes and Common Myeloid Markers in ALL

| Immuno phenotype | Lymphoid Ag | Myeloid Ag | Prognosis | Reference |
|------------------|------------------------------------|--|-----------|-----------|
| T-ALL | CD3-CD5-CD7 | CD13(12.2)-CD33(9.8)- CD14(4)-CD15(6.5)- CD11b(9.8)-CD65(10.6) | Good | (24-26) |
| B-ALL | CD19-CD20- CD22-CD34- HLA-DR | CD13(20)-CD33(16.7)- CD14(5.9)-CD15(10.8)- CD11b(6.4)-CD65(12.4) | Poor | (24 -26) |

Abbreviation: T-ALL (T cell acute lymphoblastic leukemia); B-ALL (B cell acute lymphoblastic leukemia)

Table 3. Deletion in Different Regions of Chromosome 7 in Different Types of Leukemia

| ALL | CLL | AML | CML | MDS | Reference |
|--------------|-----------|--------------|----------------|--------------|--------------|
| Del7(q11) | Del7(q11) | Del7(q11) | Del7(q11) | Del7(q11) | (28 ,27 ,22) |
| Del7(q22) | ----- | Del7(q22) | Del7(q11.2q22) | Del7(q22) | |
| Del7(q32-36) | ----- | Del7(31) | Del7(q22) | Del7(q34) | |
| Del7(p15) | ----- | Del7(q32) | ----- | Del7(q22q36) | |
| Del7(p13-15) | ----- | Del7(q34) | ----- | Del7(q35) | |
| ----- | ----- | Del7(q21) | ----- | ----- | |
| ----- | ----- | Del7(q22q32) | ----- | ----- | |
| ----- | ----- | Del7(q11q32) | ----- | ----- | |
| ----- | ----- | Del7(q22q36) | ----- | ----- | |
| ----- | ----- | Del7(q11q36) | ----- | ----- | |

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