



## Case Report

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# A Rare Case of Acute Myeloblastic Leukemia With Blast Count Less Than 20% in Bone Marrow



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## ABSTRACT

One of the diagnostic criteria for Acute Myeloblastic Leukemia (AML) is the presence of 20% myeloid blasts in peripheral blood or bone marrow. Some cases with recurrent cytogenetic abnormalities also fall in this category with blast cell count less than 20%. Thus, in the presence of these genetic abnormalities, the patients are classified as AML regardless of blast cell count. One of these genetic heterogeneities is t(8; 21) (q22, q22.1) which is more commonly seen in children and young adults. In this study, a 14-year-old boy is reported with a final diagnosis of AML, which was presented with fever and bicytopenia, clinically suspicious for acute leukemia. Laboratory results reported less than 20% blasts in bone marrow aspiration smears but genetic alteration t(8; 21) (q22, q22.1) was detected by molecular exams.

## Introduction

**A**cute Myeloid Leukemia (AML) is a type of hematologic malignancies with variable outcomes. It is characterized by a clonal proliferation of myeloid precursors who have reduced capacity to differentiate into more mature cellular elements. There is an accumulation of leukemic blasts

or immature forms in the bone marrow, peripheral blood, and occasionally in other tissues, with a variable reduction in the production of normal red blood cells, platelets, and mature granulocytes [1].

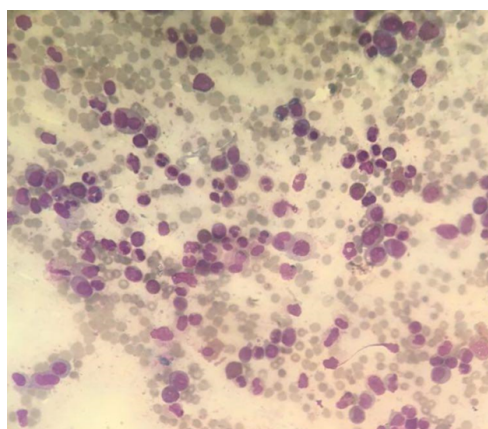
Several decades ago, the classification of AML was based on the French-American-British (FAB) Cooperative Group according to available morphologic and cytochemical char-

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**Figure 1.** Microscopic view of aspiration smears (Wright-Giemsa staining X10)

acteristics of neoplastic cells [2]. However, by recognition of various cytogenetic and molecular abnormalities and a better understanding of the AML disease biology, the World Health Organization (WHO) prompted to develop a new classification that integrated genetic, immunophenotypic, biological, and clinical features to define specific disease en-

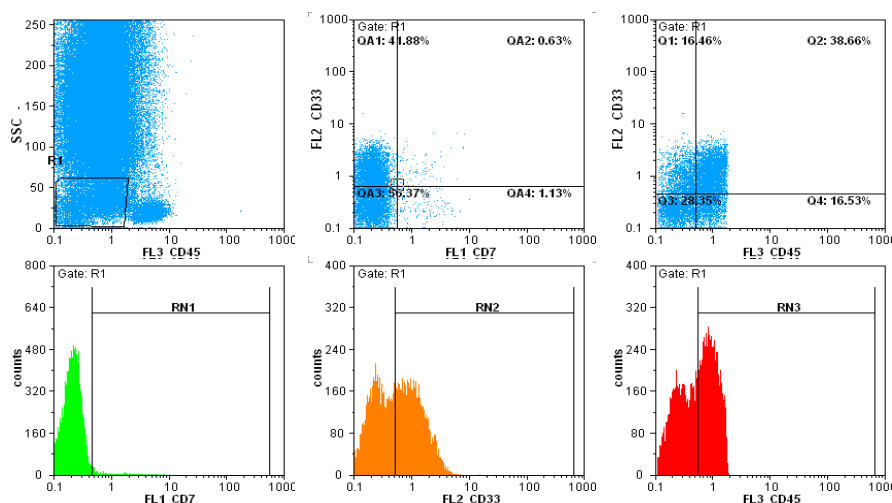
titles. The WHO classification scheme essentially replaced the FAB system with the exception that the latter remains embedded in the WHO's "AML, Not Otherwise Specified (NOS)" category [3, 4].

Acute leukemia with known chromosomal abnormality shows different clinical behavior. The translocation (8, 21) is one of the known chromosomal abnormalities in AML [5, 6]. According to the WHO classification, AML with t(8, 21) (q22, q22.1) belongs to the favorable risk group [7]. This type of AML will go into complete remission after standard chemotherapy [8]. The presence of t(8; 21) (q22, q22.1) is diagnostic of AML, even when blasts are less than 20% [9, 10].

### Case Presentation

Our patient is a 14-year-old boy presenting with fever and petechiae in upper and lower limbs for 5 days. He was referred to Omid Hospital affiliated to Isfahan University of Medical Sciences in August 2017. His lab data revealed severe leukocytosis, anemia, and moderate thrombocytopenia. Imaging study showed only mild splenomegaly.

### Analysis



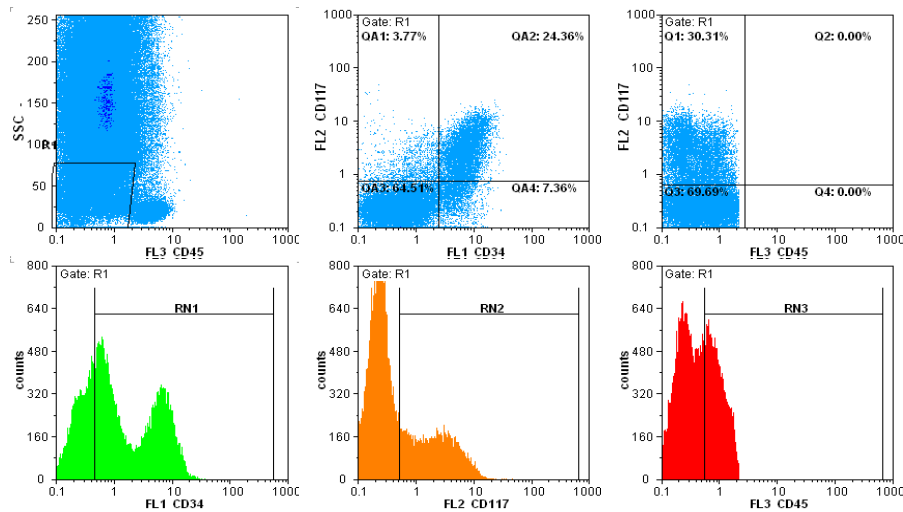
### Region Analysis

Region	Gate	Count	Count /ml	%Gated	Mean-x	CV-x%	Mean-y	CV-y%
R1	<None>	13222	-	6.66	0.69	63.36	36.34	40.93
Q1	R1	2177	-	16.46	0.35	34.03	1.15	68.99
Q2	R1	5111	-	38.66	1.03	33.02	1.29	60.62
Q3	R1	3748	-	28.35	0.27	39.79	0.23	40.53
Q4	R1	2186	-	16.53	0.95	32.89	0.28	37.56
RN1	R1	343	-	2.59	1.37	100.43	-	-
RN2	R1	6671	-	50.45	1.32	59.83	-	-
QA1	R1	5537	-	41.88	0.21	37.69	1.45	53.85
QA2	R1	83	-	0.63	1.68	91.99	1.71	71.26
QA3	R1	7453	-	56.37	0.21	38.48	0.32	50.80
QA4	R1	149	-	1.13	1.85	80.49	0.31	48.39
RN3	R1	7012	-	53.03	1.02	31.99	-	-

**Figure 2.** Multicolor flow cytometry analysis



### Analysis



### Region Analysis

Region	Gate	Count	Count /ml	%Gated	Mean-x	CV-x%	Mean-y	CV-y%
R1	<None>	37075	-	10.71	0.57	78.80	46.67	42.93
Q1	R1	11238	-	30.31	0.47	82.59	3.31	88.32
Q2	R1	0	-	0.00	-	-	-	-
Q3	R1	25837	-	69.69	0.61	76.22	0.25	47.66
Q4	R1	0	-	0.00	-	-	-	-
RN1	R1	25781	-	69.54	3.94	105.53	-	-
RN2	R1	12206	-	32.92	3.10	93.75	-	-
QA1	R1	1397	-	3.77	1.17	62.73	2.23	139.05
QA2	R1	9032	-	24.36	8.11	47.40	3.72	77.14
QA3	R1	23918	-	64.51	0.62	75.63	0.24	48.78
QA4	R1	2728	-	7.36	5.49	51.11	0.44	42.23
RN3	R1	14179	-	38.24	1.03	37.53	-	-

Figure 3. Multicolor flow cytometry analysis



Bone marrow sampling presented severe left shifted myeloid hyperplasia and 5-6% blasts in manual blast numeration (Figure 1). Multicolor flow cytometry detected about 2.6% myeloblasts with the expression of dim CD45, CD34, CD117, CD33, and MPO (Figure 2, 3). In this case, the clinical impression was acute leukemia but morphological data were not in favor of acute leukemia due to low blast cell count. Therefore, the marrow sample was sent to the molecular and cytogenetic laboratory for further investigation. Cytogenetic studies show (8; 21) (q22, q22.1) translocation and finally AML with recurrent cytogenetic abnormality was diagnosed according to WHO classification.

### Discussion

One of the diagnostic criteria of AML according to the last edition of the WHO classification of hematolymphoid malignancy is the presence of 20% myeloid blast in peripheral blood or bone marrow sample. Based on this classification, some AML with specific genetic abnormalities such as t(8; 21) (q22, q22.1), inv(16) (p13.1q22), t(15; 17) (q24.1; q21.2), and t(16; 16) (p23.1;q22) re-categorized in AML with recurrent cytogenetic abnormalities even with less than 20%

blasts in the peripheral blood or bone marrow [11]. Generally, in patients clinically suspicious for AML with laboratory reports of increase blast isolation by manual count or flow cytometry analysis, the clinician should request all genetic analysis of AML, which can be detected by Polymerase Chain Reaction (PCR), Fluorescence In Situ Hybridization (FISH), or karyotyping [12].

Obvious progress has been made in cytogenetic and molecular alteration in AML in the last four decades which has affected patients' workup suspicious for AML. Thus, the mutational profile of leukemic cells has been changed by identifying the biologically specific subgroup of disease and predicting response to therapy and survival. The patient's age at presentation has an important effect on balanced chromosomal translocation (common in children and young adults) while in older patients, AML is mostly accompanied with whole chromosome loss or gain as monosomy, trisomy, deletion or duplication [13].

One of the cytogenetic abnormalities related to AML is t(8; 21) (q22, q22.1), which results in the fusion of RUNX1 with RUNX1T1 and leads to core binding factor leukemia because of overexpression of RUNX1 [10, 11].

RUNX1 (also known as AML1, CBF $\alpha$ 2, or PEBP2 $\alpha$ B) is a type of transcription factor that regulates hematopoietic cell differentiation [14]. According to the WHO classification, AML with t(8, 21) belongs to the favorable risk group [15]. This type of AML will go into complete remission after standard chemotherapy. Treatment should be aggressive to gain complete remission [16]. So, differentiation of AML is very important. Detection of fused genes in t(8; 21) can be done by Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR), in situ hybridization, or by cytogenetic techniques [17].

To summarize, presence of t(8; 21) (q22, q22.1), inv(16) (p13.1q22), t(15; 17) (q24.1; q21.2), and t(16; 16) (p23.1:q22) are diagnostic of AML, even when blasts count appears to be less than 20%. Thus, if the clinical impression is acute leukemia, it is necessary to do diagnostic tests for the presence of recurrent cytogenetic abnormalities related to AML.

## Ethical Considerations

### Compliance with ethical guidelines

All ethical principles were considered in this article.

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### Conflict of interest

The authors declared no conflict of interest.

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