



## CASE REPORT

# Lineage Switch in Childhood Leukemia: A Case Report and Review of Literature

Shiva Nazari<sup>1</sup>, Fatemeh Malek<sup>2\*</sup>, Navid Zavvar<sup>1</sup>

<sup>1</sup>Pediatric Congenital Hematologic Disorders Research Center, Mofid Children's Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>2</sup>Pediatric Respiratory Diseases Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran

## ARTICLE INFO

### Article History:

Received: 01.05.2016

Accepted: 18.07.2016

### Keywords:

Leukemia

Children

Cell lineage

### \*Corresponding author:

Fatemeh Malek, MD

Pediatric Respiratory Diseases

Research Center, National Research

Institute of Tuberculosis and Lung

Diseases (NRITLD), Shahid Beheshti

University of Medical Sciences,

Tehran, Iran

Email: [fmalek7721@gmail.com](mailto:fmalek7721@gmail.com)

## ABSTRACT

Acute leukemia which is the most common cancer in children is a heterogeneous group of clonal malignancies. The conversion of the leukemic cell lineage during the course of the disease or later is termed lineage switch. It has been rarely reported in the literature. In leukemia lineage switch, conversions from lymphoblastic leukemia to myeloid leukemia or vice versa are reported. Herein, we report a 7-year-old child with acute lymphoblastic leukemia which switched to acute myeloid leukemia upon relapse.

Please cite this article as: Nazari S, Malek F, Zavvar N. Lineage Switch in Childhood Leukemia: A Case Report and Review of Literature. IJBC 2016; 8(3): 86-87.

## Introduction

Acute leukaemia is a heterogeneous group of clonal malignancies categorized as acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML) or mixed phenotype acute leukemia (MPAL). All subtypes have cytogenetic and molecular alterations that have prognostic implications. Lineage switch which is the conversion of the leukemic clone is known to be associated with poor prognosis.<sup>1-3</sup> There are occasional reports of switch in leukemic cell lineage (lymphoid or myeloid) through the course of the disease in the literature.<sup>1-3</sup> Distinct hypotheses have been considered to explain the lineage switch.<sup>3</sup> Here, we present the clinical and laboratory features of a case with pre B ALL who switched to AML as a relapse.

## Case Presentation

A 7-year-old boy was admitted to Mofid Children's Hospital with a history of pallor, abdominal pain, chemosis and cervical lymphadenopathy. The initial laboratory findings demonstrated a white blood cell count of  $5.3 \times 10^9/L$ , 56% Neutrophils, 44% lymphocytes, Hemoglobin 8 g/dL, and platelet  $149 \times 10^9/L$ . Bone marrow aspiration was cellular with 94% blasts which were medium-sized. Immunophenotyping was as follows: HLA-DR (71.5%), CD10 (10 %), CD19 (90%), CD20 (95 %), CD22 (43%), CD13 (2 %) and CD33 (8 %) which was in favor of B lineage acute leukemia.

Cytogenetic study was positive for t(8,14) and karyotype demonstrated 46 XY with duplication of one segment of long arm of chromosome 1. The patient was treated

with protocol for B-Cell ALL (LMB 89 Protocol). Chemotherapy was continued for three years and the patient was in complete remission. At that time, the patient developed a short period of pancytopenia whom underwent bone marrow aspiration for further evaluation. It revealed complete infiltration of blasts which according to flowcytometry was compatible with AML. Immunophenotyping was positive for CD13 (63%), CD33 (34%), CD15 (43%), HLA-DR (82%), CD117(66%), CD45(89%),c MPO(57%), CD22 (43%), CD10 (1%), CD19 (1%), CD20 (1%) which accordingly diagnosis of AML non-M3 was established. Karyotype was unsuccessful at this time. The patient received AML directed chemotherapy and also was scheduled to go through allogeneic stem cell transplantation; however, remission was not achieved and the patient died of the disease.

### Discussion

Although rarely, switches between lymphoid and myeloid lineages may occur during treatment of acute leukemias.<sup>4</sup> Among suggested hypotheses for lineage switch is a deviation in the initial leukemic clone which actually had been MPAL; hence, the first diagnosed lineage would be converted to another at a later time.<sup>4-6</sup> In other words, lineage switch could be a part of the biologic spectrum of mixed-lineage leukemias.<sup>4-7</sup> Rossi and colleagues proposed the involvement of early bipotential B-macrophage progenitors in the course of lineage switch raising the possibility that the lineage switching event would be the conclusion of the leukemogenic mutations targeting this early bi-potential progenitor cell.<sup>4-8</sup> Additionally another explanation by Strass and co-workers could be the selection of a pre-existing chemotherapy-insensitive minor population of cells of different lineage among the predominant population of leukemic blasts at diagnosis; (biphenotypic or bilineage leukemias) resulting in a resistant subclone with expression of different antigens.<sup>4,5,9</sup>

In our patient, immunophenotyping showed a new myeloid population. The emergence of chemo-resistant subclones that are undetectable by regular methods or substitution of a new leukemic clone are probably possible and neither of them could be ruled out for our patient. Cytotoxic drugs are responsible for the process of phenotypic conversion by inducing a multipotential clone or as a cause of inducing drug-resistant clones in case of multiclonal leukemia.<sup>7</sup> In a study from Argentina published in 2012, frequency of lineage switch in childhood leukemia was 0.6% ( 9 patients), which was from lymphoid to myeloid in 7 and from myeloid to lymphoid in 2 cases.<sup>4</sup> Although, the principle mechanisms involved in lineage switch continue to be unclear, plasticity of leukemic progenitors which could be multidirectional and reversible is suggested as a possible hypothesis.<sup>10</sup>

### Conclusion

We described a case of lineage switch leukemia from ALL to AML which is a rare event. Correct diagnosis

relies upon confirmation by immunophenotyping of the lineage conversion and certification that the same cytogenetic/molecular alterations remain despite the phenotypic changes. Prognosis of lineage switch leukemia is poor as our patient could not achieve a remission and dies of his disease.

**Conflict of Interest:** None declared.

### References

1. Jacoby E, Nguyen SM, Fountaine TJ, Welp K, Gryder B, Qin H, et al. CD19 CAR immune pressure induces B-precursor acute lymphoblastic leukaemia lineage switch exposing inherent leukaemic plasticity. *Nat Commun.* 2016; 7:12320. doi: 10.1038/ncomms12320.
2. Dorantes-Acosta E, Arreguin-Gonzalez F, Rodriguez-Osorio CA, Sadowinski S, Pelayo R, Medina-Sanson A. Acute myelogenous leukemia switch lineage upon relapse to acute lymphoblastic leukemia: a case report. *Cases J.* 2009; 2:154. doi: 10.1186/1757-1626-2-154. PubMed PMID: 19946525. PubMed Central PMCID: PMC2783110.
3. Imataki O, Ohnishi H, Yamaoka G, Arai T, Kitanaka A, Kubota Y, et al. Lineage switch from precursor B cell acute lymphoblastic leukemia to acute monocytic leukemia at relapse. *Int J Clin Oncol.* 2010; 15(1):112-5. doi: 10.1007/s10147-009-0007-3. PubMed PMID: 20066454.
4. Rossi JG, Bernasconi AR, Alonso CN, Rubio PL, Gallego MS, Carrara CA, et al. Lineage switch in childhood acute leukemia: An unusual event with poor outcome. *Am J Hematol.* 2012; 87(9):890-7. doi: 10.1002/ajh.23266. PubMed PMID: 22685031.
5. Stass SA, Mirro J Jr. Lineage heterogeneity in acute leukaemia: acute mixed-lineage leukaemia and lineage switch. *Clin Haematol.* 1986;15:811-27. doi: 10.1016/S0046-8177(85)80125-8. PubMed PMID: 3536242.
6. Stass S, Mirro J, Melvin S, Pui CH, Murphy SB, Williams D. Lineage switch in acute leukemia. *Blood.* 1984; 64(3): 701-6. PubMed PMID: 6590097.
7. Mura R, D'angelo P, Rizzari C, Biondi A, Giudici G, Crosti L, et al. Lineage switch in a childhood T-Cell acute lymphoblastic leukemia. *Pediatr Hematol Oncol.* 1992; 9(3):281-8. doi: 10.3109/08880019209016598.
8. Park M, Koh KN, Kim BE, Im HJ, Jang S, Park CJ, et al. Lineage switch at relapse of childhood acute leukemia: a report of four cases. *J Korean Med Sci.* 2011; 26(6): 829-31. doi: 10.3346/jkms.2011.26.6.829. PubMed Central PMCID: PMC3102880.
9. Gagnon GA, Childs CC, LeMaistre A, Keating M, Cork A, Trujillo JM, et al. Molecular heterogeneity in acute leukemia lineage switch. *Blood.* 1989; 74(6):2088-95. PubMed PMID: 2553159.
10. Dorantes-Acosta E, Pelayo R. Lineage switching in acute leukemias: a consequence of stem cell plasticity? *Bone Marrow Res.* 2012; 2012:406796. doi: 10.1155/2012/406796. PubMed PMID: 22852088. PubMed Central PMCID: PMC3407598.