# Conversion of ALL to AML: A rare phenomenon

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## ABSTRACT

Among all acute leukemias, acute lymphoblastic leukemia (ALL) is five times more common than acute myeloid leukemia (AML). Lineage switch from ALL to AML is very rare. Lineage switching is a phenomenon noted in cases of leukemias where the initially diagnosed cases of leukemias of a lineage (lymphoid/myeloid) present with the opposite lineage at relapse. Here, we report the case of a 10-year-old male child who was initially diagnosed with ALL and on relapse after 4 years, presented with AML. The blast cell morphology and immunophenotype were consistent with the diagnosis of typical AML.

**Keywords:** *Acute lymphoblastic leukemia, Acute myeloid leukemia, Flowcytometry, Lineage switch.*

Acute leukemias (AL) are the most common cancer in childhood and characterized by the uncontrolled production of hematopoietic precursor cells [1]. Although the survival rates have increased in the last few years, factors such as cell lineage switching at relapses lead to poor prognosis [2–4]. The conversions from acute lymphoblastic leukemia (ALL) to acute myeloid leukemia (AML) or vice versa are rare and recorded as lineage switching. The exact mechanisms involved in these phenomena are not well defined. The prognosis for these patients is variable, and there is no standard treatment for them. In this article, we report the case of conversion of ALL to AML in a 10-year-old male following chemotherapy.

## CASE REPORT

A 10-year-old male presented with complaints of fever for the last 3 months, progressive pallor since last 2 months, and bleeding from nose and gums since last 15 days. His appetite was decreased since last one month along with dizziness and constipation. He had received 3 units of blood, 1 week back and reported an episode of blood in stool, one-day before admission. The patient had a history of being diagnosed with ALL 4 years back. His bone marrow aspiration smears showed the presence of 95% lymphoblasts. The diagnosis of B-ALL was confirmed on flow cytometry with blasts showing positivity for CD34, CD45, CD10, CD19, CD22, CD79a. Myeloid and T-cell markers were negative. The patient had taken treatment for ALL for 3 years and remained asymptomatic for 1 year. His bone marrow examination was repeated post-treatment and smears showed features of remission with normocellular marrow and erythroid hyperplasia.

However, the patient again presented with the symptoms as reported earlier. Physical examination revealed pallor. No organomegaly was noted. Systemic examination did not reveal any gross abnormality and vitals were stable. Based on the past medical history of ALL and the presenting symptoms, a provisional diagnosis of "Acute leukemia with relapse" was made.

A proper hematological examination was advised. His complete blood count showed a hemoglobin of 5.1gm/dl, total leukocyte counts (TLC) of 9000/µL and platelet count of 20,000/µL. Peripheral smear examination showed normocytic normochromic red blood cells. A shift to the left was noted in differential leukocyte count (DLC) with the presence of 33% blasts. Bone marrow examination showed dilute marrow with scattered blasts. Flow cytometry immunophenotypic analysis was done. Blasts constituted 17% of total acquired events, showing bright positivity of CD13 and CD33 (Fig. 1A). Heterogeneous expression of HLA-DR and CD117 (Fig. 1B) was also noted along with the positivity of myeloperoxidase (Fig. 1C). Blasts showed negative expression of CD5, CD7, CD10, CD19, CD22, CD14, CD64, cCD3 (Fig. 2A-D).

Based on flow cytometric immunophenotypic findings, a diagnosis of AML at relapse was made. The flow cytometric immunophenotypic findings of the patient at two different settings

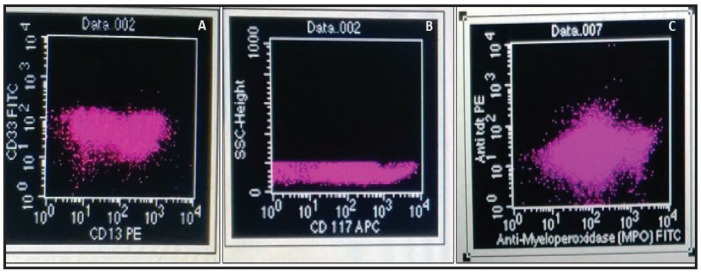


**Figure 1A-C: Flow cytometry at relapse (AML) with blast cells showing positivity for CD 13, CD33, CD117, and anti-myeloperoxidase.**

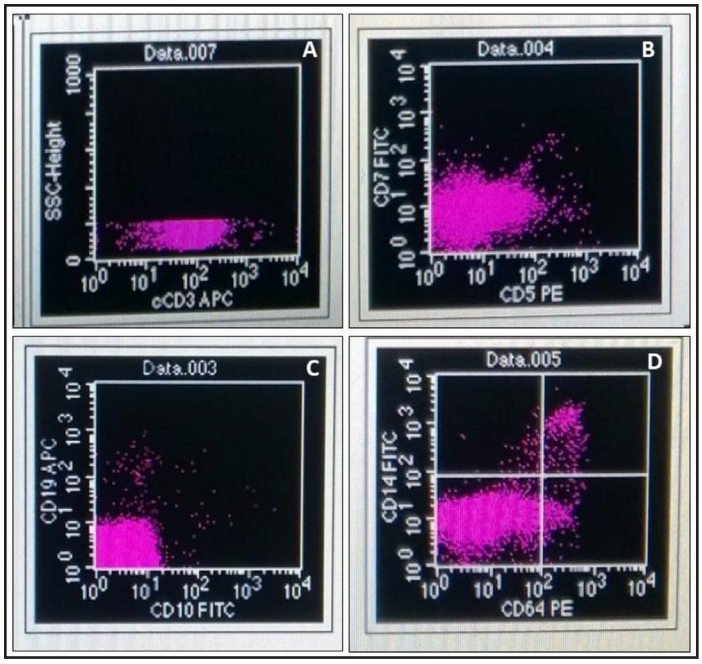


**Figure 2A-D: Flow cytometric analyses of blast cells at relapse showed negative expression of CD5, CD7, CD10, CD19, cCD3, CD14& CD64.**

have been presented in Table 1. This type of a refractory case of leukemia with lineage switch required intensive combined chemotherapy regimen; hence, the patient was referred to a higher center for further management.

## DISCUSSION

Acute leukemias (AL) are the most common cause of childhood cancer worldwide. There is uncontrolled production of hematopoietic precursor cells of the lymphoid or myeloid series within the bone marrow. It has been noted that in patients of acute leukemia, lineage switching occurs at relapse [1–4]. Lineage switching is an example of the lineage heterogeneity that exists in acute leukemias. A lineage switch may represent either a relapse of the original clone with heterogeneity at the morphological level or high plasticity attributes or the emergence of a new leukemic clone [2–6]. For example, a patient diagnosed initially with ALL is diagnosed with AML at relapse and vice versa.

Various mechanisms have been proposed to explain its etiology. Reprogramming and/or redirection of the precursor cell fate within bone marrow is considered one of the important reason behind this phenomenon [2–4]. Genetic and epigenetic changes in transcription factors of fully committed or developing cells are the basis of cellular reprogramming [3–6]. During dedifferentiation, a cellular change occurs in a differentiated state which in turn get back to a more primitive and less committed stage. Microenvironment may influence all proposed mechanisms by modulating the genome plasticity of the cells and change the leukemia outcome at relapse [5–9].

This phenomenon of lineage switch occurs when acute leukemias that meet the standard criteria for a lineage (lymphoid or myeloid) at the time of the initial diagnosis meet the criteria for the opposite lineage upon relapse [2–5]. In a study by Acosta *et al.* [4], eighteen cases of pediatric lineage switch have been reported. Conversion of ALL to AML was noted in 9 cases, AML to B-ALL in 5 cases and mixed phenotypic leukemia in 4 cases [4]. It has been noted in different studies that conversion of AML to ALL is rarer when compared to ALL to AML. Park *et al*. reported 4 cases of lineage switching in patients of ALL to AML [9]. A similar case of conversion of ALL to AML was reported by Chung *et al.* [5]. Various studies related to lineage switching in case of acute leukemias have been presented in Table 2.

The detailed analysis and classification of leukemia as per the lineage can be done by analyzing the expression of surface

**Table 1: A table comparing the Flowcytometric immunophenotypic findings of the patient at two different admissions.**

| Flow cytometric immunophenotypic findings | Diagnosed as ALL 4 years back | Diagnosed as AML (on relapse, 4 years post treatment) |
|---|---|---|
| CD34 | +ve | +ve |
| CD45 | +ve | +ve |
| CD5 | -ve | -ve |
| CD7 | -ve | -ve |
| CD10 | +ve | -ve |
| CD19 | +ve | -ve |
| CD22 | +ve | -ve |
| CD79a | +ve | -ve |
| CD13 | -ve | +ve |
| CD33 | -ve | +ve |
| CD14 | -ve | -ve |
| CD64 | -ve | -ve |
| HLA-DR | +ve | +ve |
| CD117 | -ve | +ve |
| MPO | -ve | +ve |

**Table 2: Table summarizing various studies regarding lineage switch in acute leukemia cases [1-9]**

| Authors | Diagnosis at initial presentation | Diagnosis at relapse |
|---|---|---|
| Acosta *et al.* [4], 2012 (review article) 18 cases of leukemia with lineage switch [1–9]. | ALL-L1 | AML-M5 |
| | AML-M5 | ALL-L1 |
| | AML-M5 | B-ALL |
| | B-ALL | AML-M5 |
| | Pro B-ALL | AML |
| | Pre B-ALL1 | AML-M4 |
| | ALL | AML-M5b |
| | AML | ALL-L1 |
| | Pro B-ALL L1 | AML-M0 |
| | AML-M5 | Pro B-ALL |
| | ALL-L1 | AML-M0 |
| | B-ALL-L1 | AML-M4 |
| | B ALL-L2 | T-ALL |
| | AML | ALL |
| | ALL-L1 | AML-M4 |
| | B ALL | AML M4/M5 |
| | T-ALL | AML-M0 |
| | T-ALL | AML |
| Grammatico *et al.* [7], 2013 (1 case) | Pro B-ALL | AML |
| Wu *et al.* [8], 2017 (2 cases) | 2 cases of ALL | AML-M5 and AML-M6 |
| **Current case report** | **B-ALL** | **AML** |

and cytoplasmic and nuclear antigens of leukemia cells. But, there are situations in which both lymphoid- and myeloid-lineage markers, or T-cell and B-cell markers coexist. Some 20–30% of patients with leukemia suffer relapses, during which it is common to find genetic alterations in the same original cell lineage (lymphoid or myeloid) [3–6]. In these individuals, the response to therapies for reinduction is usually of poorer quality and shorter duration.

In ALL, the most important prognostic factor is the time to relapse. A higher rate of unresponsiveness to treatment along with lower event-free survival is noted if there is an early relapse. Most relapses in AML occur during treatment within the first year upon diagnosis [5–9]. Strikingly, neonate patients that develop lineage switching, present very early relapses and poor event-free survival, that make the prognosis for these patients poor with no optimal standard treatment for them [7–9].

## CONCLUSION

Here, we present one case of lineage switch from ALL to AML. Early diagnosis is of great importance to initiate appropriate management without undue delay. Lineage switching has been reported to occur more frequently in children than adults. It is still not very clear that whether lineage switching is a feature of acute leukemia which promotes instability of hematopoietic lineage or it is the plasticity of AL genome following leukemic transformation. This phenomenon correlates with very bad prognosis and resistance to therapy; hence, further studies are appreciated to unfold the mechanisms of recurrence in cases of leukemias and possible implications for further management.

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