Clin. Lab. 2025;71:XXX-XXX

CASE REPORT

Lineage Switch from Acute Lymphoblastic Leukemia to Acute Myeloid Leukemia with PDGFRB Mutation after Allogeneic Stem Cell Transplantation

Hongjuan Yu, Xuefen Qi, Jifei Zhang, Lingrong He

Department of Clinical Laboratory, Quzhou Kecheng District People's Hospital, Quzhou, Zhejiang Province, China

SUMMARY

Background: **The goal was to investigate the clinical characteristics of acute T-lymphoblastic leukemia (T-ALL) transforming into acute myeloid leukemia (AML) and to provide a basis for improved clinical diagnosis and treatment of this condition.**
Methods: **A retrospective analysis was performed on the clinical data and treatment process of a patient with T-ALL who transitioned to AML after undergoing allogeneic hematopoietic stem cell transplantation. Relevant literature was also reviewed.**
Results: **The patient, a 24-year-old female, initially presented with fatigue. A comprehensive examination confirmed the diagnosis of T-ALL. Following induction chemotherapy, the patient achieved complete remission (CR) as determined by hematologic and cytogenetic assessments. The patient subsequently underwent allogeneic hematopoietic stem cell transplantation from a sibling donor. Six months post-transplantation, bone marrow cytology indicated a relapse, with morphology and immunophenotype consistent with AML. The patient is currently in the terminal stage of a malignant tumor, with a very poor prognosis.**
Conclusions: **Lineage switching following acute leukemia relapse is associated with a poor prognosis, necessitating treatment adjustments based on the post-relapse phenotype. Clinically, for recurrent leukemia, comprehensive evaluations-including leukemia immunophenotyping, gene mutation analysis, and cytogenetic and molecular biological examinations-are essential to better guide treatment and assess prognosis.**
(Clin. Lab. 2025;71:xx-xx. DOI: 10.7754/Clin.Lab.2024.240833)

Correspondence:
Lingrong He
No. 122, Shuanggang Avenue
Quzhou City, 324000, Zhejiang Province
China
Email: 3763580324@qq.com

Case Report accepted September 2, 2024

KEYWORDS

acute T-lymphoblastic leukemia, acute myeloid leukemia, allogeneic stem cell transplant, PDGFRB mutation

INTRODUCTION

Leukemia is a malignant clonal disorder of hematopoietic stem progenitor cells, characterized by the uncontrolled proliferation of leukemic cells and the suppression of normal hematopoiesis. Although chemotherapy combined with hematopoietic stem cell transplantation has significantly improved the prognosis for leukemia patients, many still experience relapse. Typically, the phenotype of blast cells in the bone marrow of relapsed leukemia patients is identical to that at the initial diagnosis. However, in some cases, a lineage switch occurs

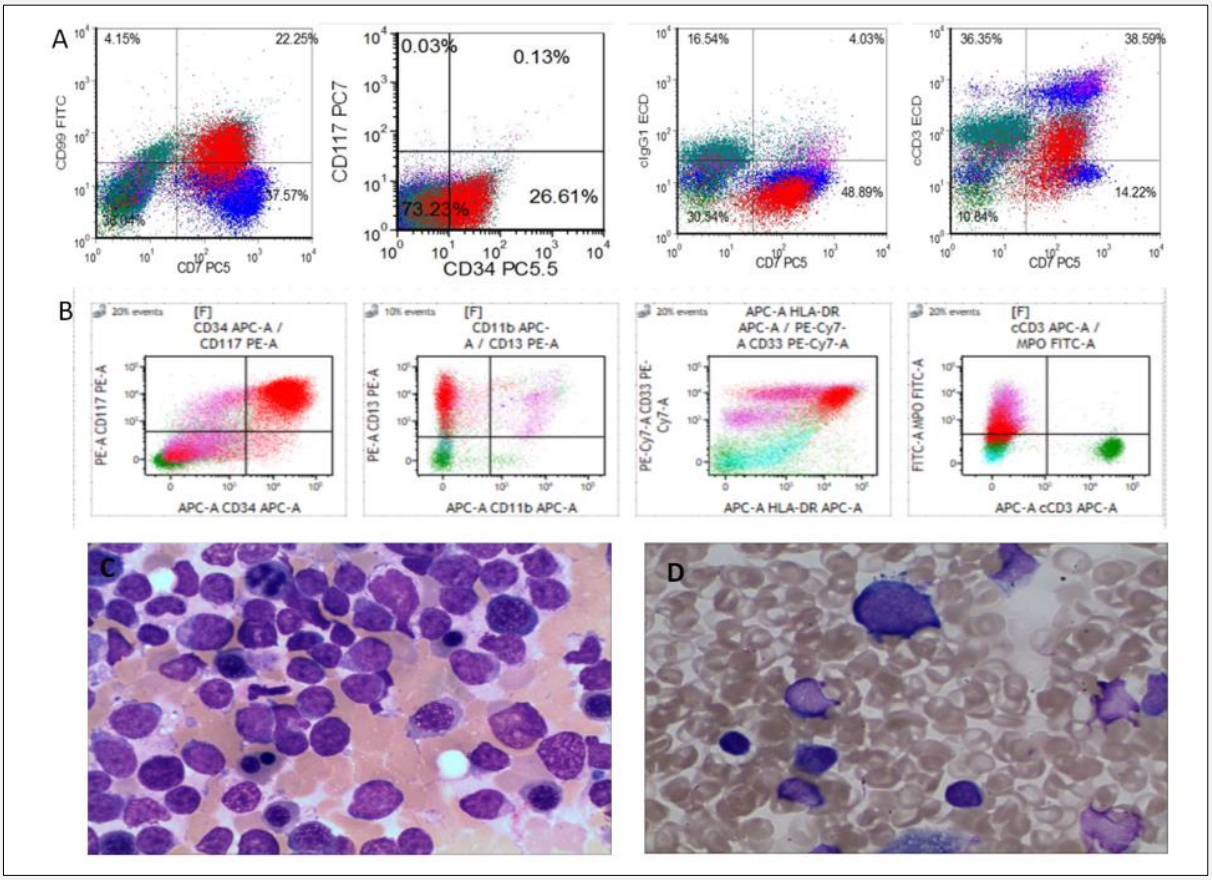

Figure 1. A) The blast population expressed T-lymphoid CD7, CD5, cCD3, CD99, and CD34 markers. B) The blast population expressed myeloid CD34, CD117, CD13, CD33, MPO markers. C) Bone marrow smear shows that 42.4% of nucleated cells were lymphoblasts, and myeloperoxidase (MPO) staining was negative. D) The peripheral blood smear shows 13% blast cells.

at relapse, where acute leukemia initially diagnosed as one type (myeloid or lymphoid) transforms into the opposite type. This phenomenon is rare, occurring in approximately 6% to 9% of cases, and is most commonly observed as a switch from B-ALL to AML, particularly in children. The lineage switch from T-ALL to AML, as observed in this case, is exceedingly rare in clinical practice.

CASE REPORT

The patient is a 24-year-old female who was admitted due to a relapse of acute T-cell lymphoblastic leukemia (T-ALL) one year after undergoing allogeneic hematopoietic stem cell transplantation. Initially, she was hospitalized a year ago with symptoms of fatigue. Upon admission, laboratory results showed a white blood cell count of 3.23 x 10^9/L, a lymphocyte count of 1.86 x 10^9/L, a hemoglobin level of 116 g/L, and a platelet count of 121 x 10^9/L. A peripheral blood smear revealed the presence of blast cells. A bone marrow smear indicated that 42.4% of nucleated cells were lymphoblasts, and myeloperoxidase (MPO) staining was negative (Figure 1C). Immunophenotyping of bone marrow cells showed that 25.3% of nucleated cells were immature T cells, characterized by CD34+, CD117-, CD33+, HLA-DR+, CD5-, CD7+, CD2-, partially CD8+, CD4-, CD 56+, cMPO-, sCD3-, cCD3+, and CD99+ (Figure 1A). Screening for 56 leukemia-related fusion genes was negative. Testing for PH-like ALL-related gene mutations showed a positive PDGFRB mutation. Cytogenetic analysis of the bone marrow revealed a karyotype of 46, XX [20]. Based on these findings, the patient was diagnosed with acute T-cell lymphoblastic leukemia. The patient underwent six courses of standardized chemotherapy, during which bone marrow cytology indicated remission. She subsequently received a sibling al-

logeneic hematopoietic stem cell transplantation. Six months post-transplantation, a peripheral blood smear showed 13% blast cells (Figure 1D), and bone marrow cytology revealed that 55% of the cells were immature blasts, with partial focal positivity for POX, suggesting an AML-M2a phenotype. Flow cytometry of the bone marrow showed that myeloid blasts accounted for 47% of non-erythroid cells, expressing CD34, CD117, CD13, CD33, HLA-DR, and MPO, while lacking expression of cCD3, cCD79a, CD10, CD19, and CD7 (Figure 1B). Integrating the results from bone marrow cytology and flow cytometry, it was concluded that the relapse of T-ALL post-transplant had transformed into acute myeloid leukemia M2a.

The patient is currently in the terminal stage of malignant disease, presenting with fever, multi-organ dysfunction, septic shock, and multiple organ failure, with a very poor prognosis.

DISCUSSION

In recent years, hematopoietic stem cell transplantation (HSCT) has demonstrated remarkable efficacy in treating acute leukemia, providing hope for patients with relapsed or refractory disease. However, research, and attention regarding lineage switches or secondary malignancies post-HSCT remain limited. Our study reports a case of a patient with T-cell acute lymphoblastic leukemia (T-ALL) who experienced a lineage switch to acute myeloid leukemia (AML). Such a transition from T-ALL to AML is clinically rare [1,2].

The pathogenesis of lineage switch in acute leukemia remains unclear, with three main hypotheses proposed: 1) At initial diagnosis, the patient may have had mixed-lineage leukemia. Chemotherapy might suppress the predominant leukemic clone identified at diagnosis, allowing the expansion of a different phenotypic subclone, thus manifesting as another type of leukemia [3]. 2) The leukemic stem cells at initial diagnosis may possess characteristics of both myeloid and lymphoid progenitors, enabling bidirectional differentiation into myeloid and lymphoid lineages [4]. 3) Similar to normal hematopoietic stem cells, leukemic cells may exhibit plasticity and reversibility [5]. The fate of these stem cells could be altered under the influence of various transcription factors or cytokines within the hematopoietic microenvironment.

After a lineage switch in leukemia, treatment should be aligned with the post-switch phenotype. However, most patients do not respond well to such treatment [6,7]. Clinically, for relapsed leukemia, comprehensive examinations including immunophenotyping, gene mutation detection, and cytogenetic and molecular biological analyses are essential to guide treatment and assess prognosis. In this case, fusion gene and relevant mutation analyses revealed only a positive PDGFRB mutation. Further research is needed to determine whether the lineage switch or the development of secondary malignancies is related to the PDGFRB mutation.

Declaration of Interest:
All authors declare no competing interests.

References:

1. Kuze A, Ida N, Hosono N, Negoro E, Yamauchi T. [Lineage switch from T-lymphoblastic leukemia to myeloid leukemia at relapse]. Rinsho Ketsueki 2021;62:721-6. (PMID: 34349054)

2. Permikin Z, Popov A, Verzhbitskaya T, et al. Lineage switch to acute myeloid leukemia during induction chemotherapy for early T-cell precursor acute lymphoblastic leukemia with the translocation t(6;11)(q27;q23)/KMT2A-AFDN: A case report. Leuk Res 2022;112:106758. (PMID: 34864370)

3. Skhoun H, Khattab M, Chebihi ZT, Belkhayat A, Dakka N, BaghdadI JE. B/T mixed phenotype acute leukemia with high hyperdiploidy and lineage switch to B-cell acute leukemia. Leuk Res Rep 2022;17:100289. (PMID: 35079568)

4. Gupta SK, Kumar R, Chharchhodawala T, Kumar L. Secondary pure erythroid leukaemia in relapsed acute lymphoblastic leukaemia: lineage switch or chemotherapy effect? BMJ Case Rep 2014;2014. (PMID: 24842350)

5. Hu T, Murdaugh R, Nakada D. Transcriptional and Microenvironmental Regulation of Lineage Ambiguity in Leukemia. Front Oncol 2017;7:268. (PMID: 29164065)

6. Semchenkova A, Mikhailova E, Komkov A, et al. Lineage Conversion in Pediatric B-Cell Precursor Acute Leukemia under Blinatumomab Therapy. Int J Mol Sci 2022;23(7):4019. (PMID: 29164065)

7. Rossi JG, Bernasconi AR, Alonso CN, et al. Lineage switch in childhood acute leukemia: an unusual event with poor outcome. Am J Hematol 2012;87:890-7. (PMID: 22685031)