Therapy-related acute myeloid leukemia following treatment of acute lymphoblastic leukemia in a child : a case report

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INTRODUCTION

Therapy-related acute myeloid leukemia (t-AML) can rarely occur in pediatric patients after chemotherapy for acute lymphoblastic leukemia (ALL), typically due to cytotoxic treatments such as alkylating agents or anthracycline.
We report a rare case of an 11-year-old boy being diagnosed with secondary acute myeloid leukemia (AML) during his maintenance phase of treatment for B-ALL, approximately 29 months after the primary diagnosis.

CASE PRESENTATION

The patient was first admitted for complaining of fever and fatigue and the appearance of a cervical lymph node. 21% lymphoid blasts were detected in blood smear and 80% on bone marrow smear.
He had a complex karyotype.
The immnuophenotype of bone marrow supported the diagnose of B-ALL.
The patient received the FRALLE 2000 protocol .
He was corticosteroid-resistant, with 53% lymphoblasts in blood smear after 8days with corticotherapy, and chemo-sensitive with a complete remission after induction .
When he was admitted to receive 5th cure of maintenance , he presented swelling tonsils , fever and sever anemia. The blood test showed profound pancytopenia.
Bone marrow examination showed increased blasts (23% of blasts).
Flow cytometry analysis demonstrated positive expression of HLA-DR, cTdT, cMPO, cCD79a, CD14, CD13, CD33, CD11c, CD117, CD64, CD36, CD38, CD123 and CD4, on the surface of these blasts wich supported the diagnosis of Acute monocytic leukemia. He was diagnosed with t-AML.
The patient underwent induction chemotherapy with anthracyclines and cytarabine (3+7) . Bone marrow after induction showed 28% of blasts.
He then received intensification IDAC (intermediate-dose cytarabine) .
the bone marrow results was in favor of complet remission.

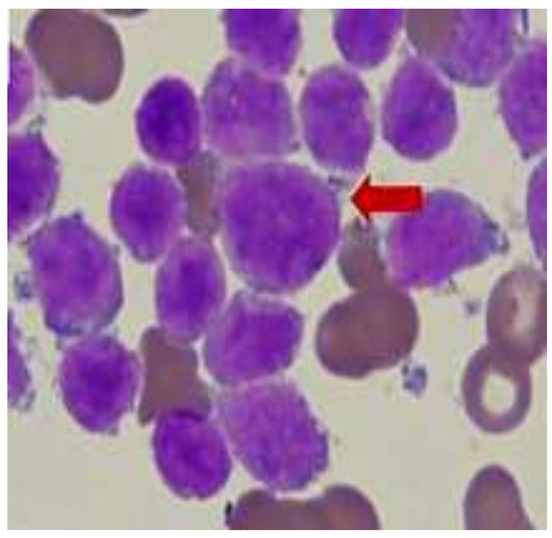

Figure 1 : Typical lymphoblastic cells with large hyperchromatic and prominent nucleoli

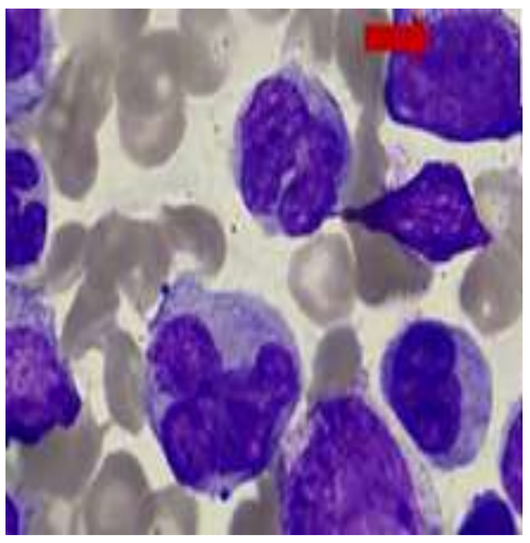

Figure 2 : Morphologic findings of secondary AML
Typical myeloblastic cells with large hyperchromatic and prominent nucleoli

DISCUSSION

ALL is the most common hematologic cancer, with a survival rate around 90%. The development of t-AML is often linked to prior hematologic disorders or exposure to chemotherapy. T-AML to alkylating agents typically involves deletions on chromosomes 5 or 7, a 5–7 year latency, and a history of myelodysplasia. In contrast, secondary AML related to topoisomerase II inhibitors shows 11q23/KMT2A alterations and a shorter latency of 1–2 years.
This patient received doxorubicin, cyclophosphamide, vincristine, methotrexate, and cytarabine, and developed t-AML 29 months after the initial diagnosis. The combination of alkylating agents and topoisomerase II inhibitors may contribute to early transformation in children.
Clonal hematopoiesis with driver mutations, altered drug metabolism, and DNA repair defects are key risk factors for therapy-related AML. Recent studies highlight that clonal hematopoiesis with driver mutations, in combination with variations in cytotoxic drug metabolism and DNA repair capacity, are significant risk factors for therapy-related AML (t-AML). It is suspected that chemotherapy-induced mutations in key genes played a role in the development of t-AML in this patient.
Unfortunately, molecular analysis was not performed due to financial limitations.

CONCLUSION

In conclusion, t-AML in pediatric patients is uncommon during treatment for primary ALL. The early-onset sAML observed in our patient may be a result of the aggressive induction therapy involving alkylating agents and TOPII . Being aware of this adverse effect can help identify the increased risk of secondary malignancies, and adjust to different therapeutic regimen

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