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ETUDE DE CAS

Treatment of Relapsed Early T-Cell Precursor Acute Lymphoblastic Leukemia with Venetoclax.

Traitement de la leucémie aiguë lymphoblastique à précurseurs T précoces en rechute avec le vénétoclax.

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Résumé

La leucémie lymphoblastique aiguë à précurseurs T précoces est une entité biologiquement distincte (LAL- PTP) dans la classification OMS 2022 , et est associée à un mauvais pronostic en raison de sa résistance à la chimiothérapie et de son taux élevé de rechute. Cibler les protéines oncogènes de la famille BCL-2 avec des agents tels que le vénétoclax offre une alternative thérapeutique aux patients atteints d'une maladie réfractaire ou en rechute. Dans ce rapport de cas, nous décrivons un patient atteint d'une LAL-PTP en rechute et réfractaire, traité par une courte cure de vénétoclax. Ce traitement s'est avéré efficace et peut permettre aux patients répondeurs d'accéder à une greffe de cellules souches allogéniques.

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Mots clés : Leucémie lymphoblastique aiguë à précurseurs T précoces, LAL-PTP, vénétoclax.

Abstract

Early T-cell precursor acute lymphoblastic leukemia (ETP-ALL) is a biologically distinct entity in the 2022 WHO classification and is associated with a poor prognosis due to its resistance to chemotherapy and high relapse rate. Targeting oncogenic proteins of the BCL-2 family with agents such as Venetoclax offers a therapeutic alternative for patients with refractory or relapsed disease. In this case report, we describe a patient with relapsed disease refractory to standard treatment, who was managed with a short course of Venetoclax.

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keywords: Early T-cell precursor, acute lymphoblastic, leukemia , ETP-ALL, Venetoclax.

Introduction

Early T-cell precursor acute lymphoblastic leukemia (ETP-ALL) is a recently identified high-risk subtype of T-cell ALL, distinguished by early differentiation arrest and unique genetic and transcriptional profiles. Accounting for 10–30% of adult T-ALL cases and 10–15% in children, ETP-ALL is associated with poor chemotherapy responses and high relapse rates. Relapsed or refractory ETP-ALL carries a particularly poor prognosis. Recent studies using BH3 profiling have revealed a dependence on BCL-2, with ETP-ALL cells

exhibiting marked in vitro sensitivity to the BCL-2–selective antagonist venetoclax. We report the case of a patient with relapsed ETP-ALL who responded favorably to venetoclax combined with chemotherapy.

Case Report

A 25-year-old woman was diagnosed with ETP-ALL in May 2023. Bone marrow aspiration revealed 45% blasts (figure 01) , and immunophenotyping showed CD45+,

CD5+, CD7+, CD1a-, CD8-, CD3-, with aberrant expression of CD117+ and CD33+. She was treated with the BFM protocol and achieved complete remission (CR) by day 22. Consolidation therapy included Aracytine/Etoposide and Cyclophosphamide/Vincristine/Daunorubicin, followed by maintenance with Methotrexate and 6-Mercaptopurine.

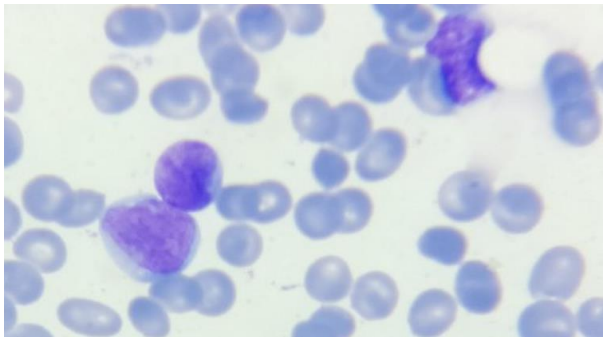


Figure 01 : showing ETP ALL blasts in bone marrow.

In February 2025, the patient developed persistent cytopenias and peripheral lymphadenopathy. Bone marrow analysis confirmed relapse with 64% blasts exhibiting the same ETP markers. She received VBAP salvage chemotherapy (Vinblastine, Etoposide, Cytarabine) but developed neutropenia and an infection requiring hospitalization. Bone marrow evaluation indicated treatment failure with 58% blasts. Subsequently, she was treated with one cycle of Hyper-CVAD combined with venetoclax at 100 mg daily for 10 days, and antifungal prophylaxis with Posaconazole. No clinical or laboratory evidence of tumor lysis syndrome was observed. Post-treatment evaluation showed normalization of blood counts and a reduction of bone marrow blasts to 4%. The patient was referred for allogeneic hematopoietic stem cell transplantation.

Discussion

Our patient was successfully managed with Venetoclax in combination with chemotherapy, and then bridged to allogeneic haematopoietic stem cell transplantation (Allo-HSCT). Preclinical investigations suggest that the modulation of apoptotic pathways may be beneficial in the treatment of ETP-ALL [1].

ETP-ALL is characterized by elevated expression of BCL-2, rendering it particularly responsive to BCL-2 inhibition. Venetoclax, used as a monotherapy, has demonstrated effects on the proliferation of human T-ALL cell lines and immature cells, notably those exhibiting the ETP phenotype [2,3].

The first case of ETP-ALL treated with Venetoclax was documented in 2018 [4]: this case involved a 71-year-old female patient who exhibited resistance to four prior treatment regimens (Hyper-CVAD, Nelarabine, liposomal vincristine, Palbociclib and Methotrexate), and subsequently achieved complete remission through the administration of Venetoclax combined with attenuated mini-CVD chemotherapy. A recent publication reported a series of five patients with relapsed or refractory ETP-ALL, and who underwent salvage treatment with Venetoclax in combination with an hypomethylating agent (Decitabine or Azacitidine): three patients attained CR, while one experienced a significant reduction in blast count [5].

To mitigate the risk of tumor lysis syndrome, Venetoclax is administered in a ramp dosing regimen: 100 mg on the first day, 200 mg on the second day, and 400 mg on the third day [6].

The dosage of Venetoclax is further adjusted to 50 mg-100 mg per day when co-administered with Posaconazole [7]. Our patient commenced treatment with an initial dose of 100 mg of Venetoclax combined with Posaconazole, without the onset of tumor lysis syndrome, maintaining an acceptable hematological safety profile.

In the series described by Agrawal et al. [5], the duration of Venetoclax administration varied from 14 to 28 days: one patient received treatment for 14 days, two patients for 21 days, and the fifth for 28 days. In the same cohort, two patients in remission underwent allogeneic hematopoietic stem cell transplantation. Our patient was received a shorter course of Venetoclax, for only 10 days, after which she was considered for allogeneic transplantation.

Conclusion

This case supports the use of venetoclax combined with chemotherapy as a salvage therapy in relapsed ETP-ALL, facilitating remission and enabling subsequent allogeneic stem cell transplantation. Further studies are warranted to establish standardized treatment protocols.

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