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Successful CPX-351 treatment of seminoma therapy-related acute myeloid leukemia in a patient with Klinefelter syndrome

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Introduction

We present a case report of the successful use of CPX-351, a liposomal formulation of cytosine arabinoside and daunorubicin with an appropriate molar ratio of these agents (amounting to 5:1) [1], in an AML patient with Klinefelter syndrome previously treated for seminoma. Therapy-related acute myeloid leukemia (t-AML) is a severe long-term complication of cancer treatment. As patient survival rates increase, the incidence of such distant complications becomes more significant. Both radiation and cytotoxic drugs used in cancer therapy are mutagenic, with the risk of developing t-AML estimated in some studies to be up to 1% per year. Additionally, t-AML tends to be more resistant to treatment compared to primary leukemia, and patients are often more susceptible to adverse effects due to their previous exposure to cytotoxic therapies. Therefore, it is crucial to explore novel and less toxic treatment options.

Case report

A 56-year-old male was admitted to the Hematology Clinic in May 2023 due to hyperleukocytosis of 105 × 10^9/L, thrombocytopenia 23 × 10^9/L, and hemoglobin 8.1 g/dL. Most of the leukocytes were myeloblasts. Physical examination revealed gingival overgrowth (Figure 1) and thrombocytopenic purpura in the upper and lower limbs. It was found that the patient at age 29 had been treated for mediastinal seminoma using BEP protocol (bleomycin, etoposide, cisplatin), followed by radiotherapy to the mediastinal area. Additionally, the patient had been under hepatological care due to liver cirrhosis secondary to HBV infection. Bone marrow aspiration revealed infiltration of myeloblasts at 89%. Immunophenotypic analysis confirmed the diagnosis of acute myeloid leukemia. Karyotype analysis revealed a male karyotype with an additional X chromosome, confirming Klinefelter syndrome. Molecular analysis revealed the presence of mutations in NPM1, FLT3-TKD, and KMT2A. Considering the history of prior intensive chemotherapy, including a topoisomerase II inhibitor, and radiotherapy, therapy-related AML (t-AML) was diagnosed.

Due to hyperleukocytosis, leukapheresis was performed, followed by subcutaneous administration of cytarabine at a dose of 100 mg. Then CPX-351 treatment was initiated at a dose of 44 mg/m^2 + 100 mg/m^2 on days 1, 3 and 5 [2, 3]. The treatment was complicated by inflammatory changes in the oral mucosa around a decayed tooth (Figure 2) that responded to antibiotics and local intervention by the surgeon. The patient remained in grade IV neutropenia until day 38 of induction chemotherapy. After hematopoietic recovery, bone marrow aspirate evaluation revealed complete remission, with minimal residual disease (MRD) at 0.003%. Subsequent remission consolidation treatment with CPX-351 at a dose of 29 mg/m^2 + 65 mg/m^2

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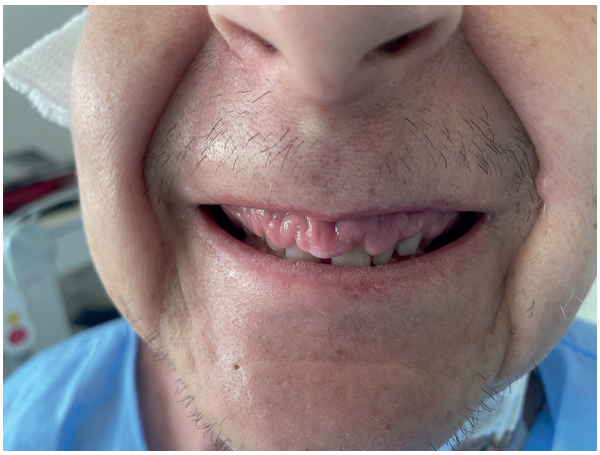

Figure 1. Gingival overgrowth

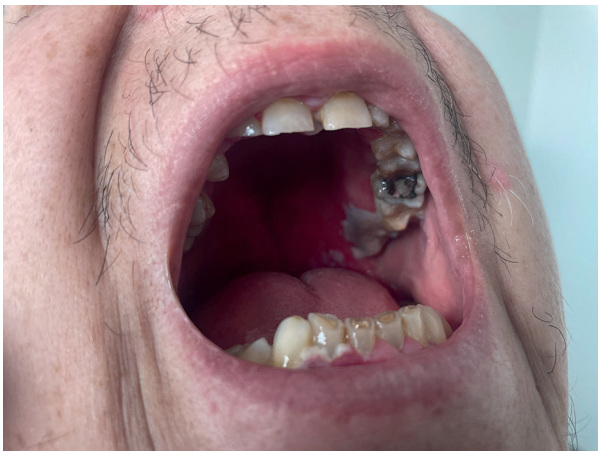

Figure 2. Gingival inflamation

on days 1 and 3 was complicated by third-degree atrioventricular block. After platelet concentrate transfusion, a DDD pacemaker was implanted, resulting in complete relief of symptoms. Since then, the patient has remained in remission, receiving maintenance therapy with oral azacitidine. Because of the heightened risk according to the Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI) score of 7 points, allogeneic stem cell transplantation was not considered.

Discussion

Klinefelter syndrome is known to increase the risk of germ cell tumors, such as mediastinal seminoma, but its association with an increased risk of acute leukemia has not been confirmed [4]. Intensive treatment with a topoisomerase II inhibitor (etoposide) and radiotherapy both increase the likelihood of developing acute myeloid leukemia in the future [5]. Prognosis in this patient group is worse than in *de novo* AML, and the search for new treatment methods offers a chance to improve the prognosis. There are several advantages of replacing a classical 3+7 regimen with CPX-351: CPX-351 vs. 3+7 in a double-blind randomized study prolonged overall survival (41.5% vs. 27.6%) and provided a higher rate of complete remissions (47.7% vs. 33.3%), as well as extended progression-free survival (6.93 vs. 6.11 months) [1, 6]. However, the use of this drug has been shown to prolong the duration of neutropenia (36 vs. 29 days) [2], resulting in an increased frequency of complications such as bleeding or pneumonia.

CPX-351 is a therapy that can be considered as one of the therapeutic options in patients with t-AML.

It is worth emphasizing that cancer survivors after potentially mutagenic therapy should be followed up at least once a year for the development of late complications such as secondary neoplasia. Although the described case is unique, the conclusions to be drawn from it have general significance for clinical practice.

Article information and declarations

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Authors contributions

NBW — manuscript preparation, data collection. WWJ — coordination, conceptualization, language edition. AL — data collection. PP — drafted manuscript and revised it critically for important intellectual content. KBJ — conceptualization, language edition, final approval.

Conflict of interest

The authors declare no conflict of interests.

Ethics statement

The authors obtained patient informed consent for publication.

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Supplementary material

None.

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