Acute and Persistent Remission of Aggressive Natural Killer Cell Leukemia in an Older Patient Induced by Chidamide Combined with Cyclophosphamide, Vindesine, Prednisone, and Etoposide Therapy

Yaşlı Bir Hastadaki Agresif Doğal Öldürücü Hücre Lösemi'sinde, Chidamide'in Siklofosfamid, Vindesin, Prednizon ve Etoposid İndüksiyon Tedavisine eklenmesiyle Akut ve Kalıcı Remisyon Sağlanması

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To the Editor,

Aggressive natural killer cell leukemia (ANKL) is a fulminant disease with a median overall survival of 2 months [1,2]. Although induction therapy with an L-asparaginase-based combined chemotherapy regimen followed by allogeneic hematologic stem cell transplantation improves clinical survival, the overall success of this approach appears rather limited [3,4]. This limitation is even more pronounced in older patients who are unable to tolerate intensive chemotherapy. Histone deacetylase inhibitors have been identified by Dufva et al. [5] as ideal drug candidates in the management of ANKL. Here we report a case of an older patient with ANKL who was treated successfully with chidamide combined with conventional chemotherapy with no significant toxicity arising.

In October 2022, a 79-year-old woman presented with a 1-month history of high fever, night sweats, and fatigue and was admitted to our hospital. Physical examination revealed hepatosplenomegaly and lymphadenopathy. Laboratory examination showed anemia, thrombocytopenia, and hypofibrinogenemia, as well as elevated bilirubin, lactic dehydrogenase, ferritin, β2-microglobulin, and interleukin-6 levels. The patient was found to be positive for Epstein-Barr virus (EBV) DNA. Bone marrow revealed 29% atypical lymphocytes with distinct granules. Flow cytometry revealed a population of cells with CD56, CD7, and CD2 positivity. Rearrangement analysis of the T-cell receptors of these cells yielded negative results, while immunohistochemical stains of bone marrow samples showed positive EBER. Karyotype analysis revealed a normal karyogram. Thus, the diagnostic criteria of ANKL were met.

Our patient received combination chemotherapy, including oral chidamide (5 mg orally every other day) and a reduced-dose COPE regimen (cyclophosphamide at 400 mg/m^2 for 1 day, vincristine at 2 mg/m^2 for 1 day, prednisone at 60 mg for 5 days, and etoposide at 100 mg for 2 days). Remarkably, the patient achieved complete remission (CR) 1 month after the initiation of induction therapy with no evidence of minimal residual disease. Stepwise laboratory examination improvement was recorded and the EBV titer turned negative. Following the completion of 7 cycles of combination therapy, which was identical to the induction regimen and was repeated every 21 days, the patient achieved sustained CR. The primary side effect observed was neutropenia, which was manageable during the combination therapy. Notably, no non-hematological adverse events, such as rashes or liver and kidney damage, occurred. As of July 2023, the patient has remained on chidamide and has shown no clinical signs of ANKL during the 4-month follow-up period.

The grave prognosis of ANKL makes it of paramount importance to explore novel therapeutic approaches. In particular, older patients, such as the one described in this report, have limited therapeutic options. Our report suggests the promising efficacy of combining chidamide with chemotherapy to treat ANKL in a manner that achieves excellent short-term outcomes and poses very few risks. Nevertheless, more questions remain unanswered regarding their role in clinical settings. How long will remission last? Should chidamide be used after chemotherapy as maintenance therapy to prevent relapse? Further investigations to evaluate the effectiveness of a chidamide-based combination strategy are warranted.

Keywords: Chidamide, Older patient, Aggressive natural killer cell leukemia

Anahtar Sözcükler: Chidamide, Yaşlı hasta, Agresif doğal öldürücü hücre lösemi

Ethics

Informed Consent: Written informed consent was obtained from the patient for publication of this case report.

Authorship Contributions

Concept- Q.L., R.P., Y.L.; Design- Q.L., R.P., Y.L.; Data Collection or Processing- Q.L., R.P., Y.L.; Analysis or Interpretation- Q.L., R.P., Y.L.; Literature Search- Q.L., R.P., Y.L.; Writing- Q.L., R.P., Y.L.

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