

Long-Term Response to Single-Agent Lenalidomide in an Elderly Patient with Relapsed Hepatosplenic T-Cell Lymphoma

Nüks Hepatosplenik T-Hücreli Lenfomalı Yaşlı Bir Hastada Tek Ajan Lenalidomide Uzun Dönem Yanıt

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To the Editor,

Hepatosplenic T-cell lymphoma (HSTCL) is a rare, aggressive peripheral T-cell lymphoma (PTCL) subtype with limited treatment options, especially in elderly patients. We report a relapsed HSTCL case in an elderly patient who achieved long-term remission with single-agent lenalidomide.

A 75-year-old male patient presented with fatigue in February 2019 and laboratory tests revealed pancytopenia. Abdominal ultrasound showed multiple nodular lesions in the liver, the largest measuring 3 cm. Positron emission tomography-computed tomography (PET-CT) revealed multiple hypermetabolic nodules in all liver segments and increased lymph node uptake in the portal hilum, pancreatoduodenal region, mediastinum, and bilateral hilar and subcarinal areas. Liver and bone marrow biopsies confirmed stage IV HSTCL. Immunohistochemical analysis demonstrated that the neoplastic cells were atypical lymphoid cells exhibiting positivity for CD3, perforin, and granzyme, while they were negative for CD20, CD30, CD4, CD8, CD5, CD2, CD56, CD57, and EBER. The Ki-67 proliferation index was approximately 80%, indicating a high level of proliferative activity. Due to his advanced age, a dose-reduced ICE (ifosfamide, carboplatin, etoposide) chemotherapy protocol was initiated. Febrile neutropenia developed after the first cycle, but subsequent cycles were completed without complications. Interim PET-CT performed on 2 May 2019, after 3 cycles of ICE, showed complete remission (CR). Chemotherapy was completed with a total of 6 cycles. A PET-CT scan performed on 22 July 2019 to assess response at the end of treatment showed durable CR. As the patient was ineligible for stem cell transplantation, maintenance pralatrexate was started. With off-label approval, the patient received a total of six cycles

administered subcutaneously at a dose of 30 mg/m² weekly in 7-week regimens. However, a PET-CT scan on 24 January 2020 showed disease progression. An off-label application for single-agent lenalidomide was submitted. One cycle of gemcitabine-vinorelbine was administered while awaiting approval. After approval, treatment was continued with lenalidomide at a dose of 25 mg/day orally for 21 days of a 28-day cycle (from day 1 to day 21, followed by 7 days off). Considering the patient's advanced age, accompanying comorbidities, and the ease of administration, it was decided to continue treatment with single-agent lenalidomide. On 12 June 2020, during the fourth month of lenalidomide treatment, PET-CT showed CR (Figure 1). The patient tolerated the therapy well and no hematological or non-hematological complications were observed. He remained in CR on lenalidomide for 2 years. However, at the end of the second year, while still in CR, he died of coronavirus disease 2019 infection.

Lenalidomide is an oral agent with immunomodulatory, antiangiogenic, and antitumor effects, and it has shown efficacy in several T-cell lymphoma (TCL) subtypes, particularly in patients ineligible for transplantation [1,2]. In a phase II study by Toumishey et al. [3], the overall response rate was 26% (8% complete, 18% partial) among 39 patients, including two with HSTCL; however, no objective responses were observed in the HSTCL subgroup. A recent phase II study assessed lenalidomide maintenance after salvage therapy in relapsed/refractory (R/R) PTCL. Among 58 patients, only two had HSTCL. The overall 1-year progression-free survival rate was 49%, though outcomes specific to the HSTCL subgroup were not reported [4]. Lenalidomide has shown clinical activity in R/R PTCL. In the multicenter phase II EXPECT trial, lenalidomide monotherapy demonstrated efficacy and safety in heavily pretreated patients, although no HSTCL

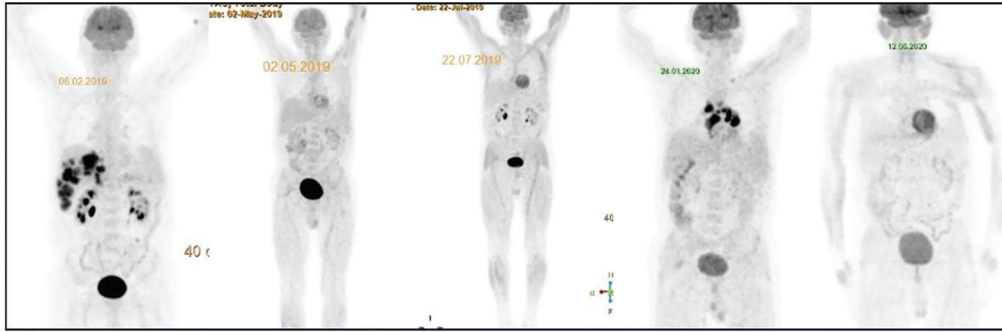


Figure 1. In June 2020, during the fourth month of lenalidomide treatment, positron emission tomography-computed tomography showed complete remission.

cases were included [5]. Other studies have reported overall response rates between 10% and 43% in R/R TCL, with a generally manageable toxicity profile [2].

Although data on HSTCL are limited, the nearly 2-year CR achieved with single-agent lenalidomide in our case despite poor prognostic factors including advanced age, bone marrow involvement, and relapsed disease highlights lenalidomide's potential efficacy. This case supports the use of lenalidomide as a viable option for aggressive lymphoma subtypes like HSTCL, especially for patients ineligible for intensive therapy. The low incidence of the disease limits robust trial data and complicates the evaluation of treatment efficacy in broader populations. In conclusion, this case highlights the potential of lenalidomide as a promising option for HSTCL, particularly in situations where standard treatments cannot be administered or are contraindicated.

Keywords: Hepatosplenic T-cell lymphoma, Lenalidomide, Peripheral T-cell lymphoma, Elderly patient

Anahtar Sözcükler: Hepatosplenik T-hücreli lenfoma, Lenalidomid, Periferik T-hücreli lenfoma, Yaşlı hasta

Ethics

Informed Consent: Informed consent for publication was obtained from the patient's family.

Footnotes

Authorship Contributions

Surgical and Medical Practices: G.A., A.H.A., S.Ç.; Concept: S.Y.K.; Design: R.A., S.Y.K., L.K.; Data Collection or Processing: G.A.,

A.H.A., S.Ç.; Analysis or Interpretation: S.Y.K., L.K.; Literature Search: R.A., S.Y.K.; Writing: R.A., S.Y.K., L.K.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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Received/Geliş tarihi: June 21, 2025
Accepted/Kabul tarihi: August 26, 2025
Epub: August 27, 2025
DOI: 10.4274/tjh.galenos.2025.2025.0252



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