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

Süreyya Yiğit Kaya[1], Rima Akil[1], Gülşah Akyol[2], Amir Hossein Abedi[3], Serhat Çelik[4], Leylagül Kaynar[1]
[1]İstanbul Medipol University Faculty of Medicine, Department of Hematology, İstanbul, Türkiye
[2]Erciyes University Faculty of Medicine, Department of Hematology, Kayseri, Türkiye
[3]İstanbul Medipol University Faculty of Medicine, Department of Internal Medicine, İstanbul, Türkiye
[4]Yıldırım Beyazıt University, Yenimahalle Training and Research Hospital, Department of Hematology, Ankara, Türkiye

Süreyya Yiğit Kaya, M.D., İstanbul Medipol University Faculty of Medicine, Department of Hematology, İstanbul, Türkiye
sureyyayigitkaya@hotmail.com
0000-0001-6732-8068

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Dear 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 intense 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 negative for CD20, CD30, CD4, CD8, CD5, CD2, CD56, CD57, and EBER. The Ki-67 proliferation index was approximately 80%, indicating a high 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. An interim PET-CT performed on 2 May 2019, after 3 cycles of ICE, showed a 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 a durable CR. As the patient was ineligible for SCT, 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 a 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 two years. However, at the end of the second year, while still in CR, he died of COVID-19 infection.

Lenalidomide is an oral agent with immunomodulatory, antiangiogenic, and antitumor effects, and 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., 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 [3]. 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, though no HSTCL 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].

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Although data on HSTCL are limited, the nearly two-year CR achieved with single-agent lenalidomide in our case—despite poor prognostic factors like advanced age, bone marrow involvement and relapsed disease—highlights its potential efficacy. This supports lenalidomide as a viable option in 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

Ethics:

Ethics Committee Approval

This article does not contain any studies with human participants or animals performed by any of the authors. This study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.

Informed consent

Informed consent for publication was obtained from the patient's family. All the authors have reviewed the manuscript and approved it for publication.

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

The authors declare that they have no conflict of interest.

Financial Disclosure

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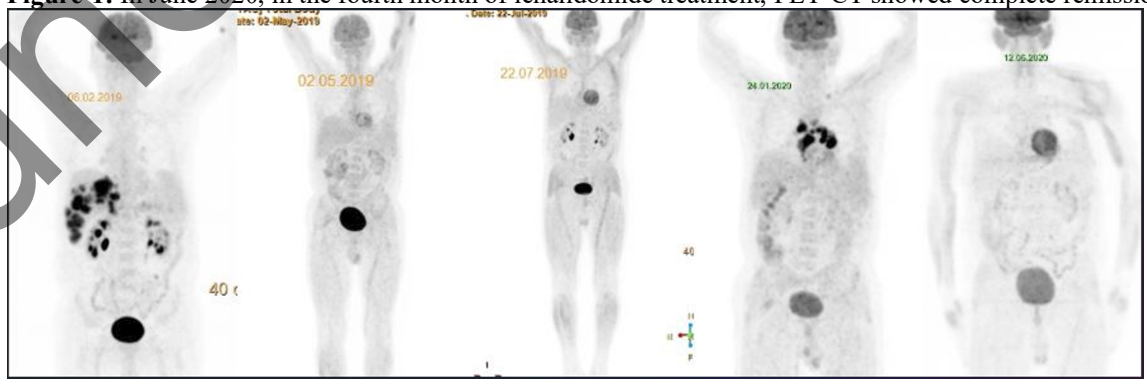
Figure-1: In June 2020, in the fourth month of lenalidomide treatment, PET-CT showed complete remission.



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