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Assessment of the efficiency of Brentuximab Vedotin in patients with pulmonary Hodgkin Lymphoma by the mean of neutrophil to lymphocyte ratio

Gokhan Erdem [a], Nuri Karadurmus [b, *], Sukru Ozaydin [b], Ibrahim Demirci [c], Bilgin Bahadir Basgoz [d], İsmail Ertürk [b], Birol Yıldız [b], Ramzan Ocal [e], Fikret Arpaci [a]

[a] Liv Hospital, Department of Medical Oncology, Ankara, Turkey
[b] University of Health Sciences, Gulhane Training and Research Hospital, Department of Medical Oncology, Ankara, Turkey
[c] University of Health Sciences, Gulhane Training and Research Hospital, Department of Endocrinology, Ankara, Turkey
[d] University of Health Sciences, Gulhane Training and Research Hospital, Department of Internal Medicine, Ankara, Turkey
[e] Gazi University, Department of Hematology, Ankara, Turkey

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ABSTRACT

Background: Lung involvement, an uncommon initial presentation of Hodgkin Lymphoma (HL), may appear as primary or secondary pulmonary HL. Although the combination of Brentuximab vedotin (BV) with AVD is suggested as an alternative treatment to combinations including bleomycin for patients with pulmonary involvement. The efficacy and adverse effects of BV have not been specialized on pulmonary HL. There is insufficient data about neutrophil to lymphocyte ratio (NLR) of cases treated with BV. We performed this retrospective study to evaluate the efficacy and toxicity of BV in patients with pulmonary HL and to demonstrate the prognostic role of NLR in patients treated with BV.

Methods: Data of 10 CD 30 (+) HL patients who treated with BV between years 2011–2016 were analyzed retrospectively. Relapsed cases after autologous bone marrow transplantation (ABMT) and/or resistant cases to at least two lines of chemotherapy, and treated with BV were included in the study.

Results: Patients underwent a median of 8.5 cycles BV. Eight patients (80%) achieved an objective response including 2 of them (20%) with complete response and six of them (60%) with a partial response at the end of the 3rd cycle. At a median follow-up of 16.8 months, median progression-free survival for all patients was 6 months and 3 patients died because of progression. BV, as a single agent, revealed well response in HL cases with pulmonary involvement and other clinical types. No pulmonary toxicity has been occurred due to BV. NLR was found to be o good indicator of prognosis and mortality in pulmonary HL patients and other HL patients. While NLR was not influenced by BV, it can be suggested as an easy prognostic marker in patients treated with BV.

Conclusion: BV may be used as a bridge therapy to the next curative treatment in order to obtain minimal tumor burden in pulmonary HL patients, and NLR can be used as a prognostic marker in these patients. We believe that this study contributes the current literature in terms of being the first research on the referred issue.

1. Introduction

Hodgkin Lymphoma (HL) is a malignant lymphoid neoplasia, characterized by the presence of malignant Hodgkin-Reed Sternberg (HRS) cells.[1] Lung involvement as initial presentation is uncommon for HL (approximately 12%).[2] Lung involvement may present as secondary or primary pulmonary HL. Secondary pulmonary HL is observed in 15–40% of the HL cases, usually, at stages III and IV. On the other hand, primary pulmonary HL is an unusual presentation with less than 100 cases reported worldwide.[3,4] (see Fig. 1)

Multidrug chemotherapy, alone or combined with radiotherapy, provided a curative treatment opportunity in 70–80% of patients.[5]

* Corresponding author. University of Health Sciences, Gulhane Training and Research Hospital, Department of Medical Oncology, 06010, Ankara, Turkey.;
E-mail address: drnkaradurmus@yahoo.com (N. Karadurmus).
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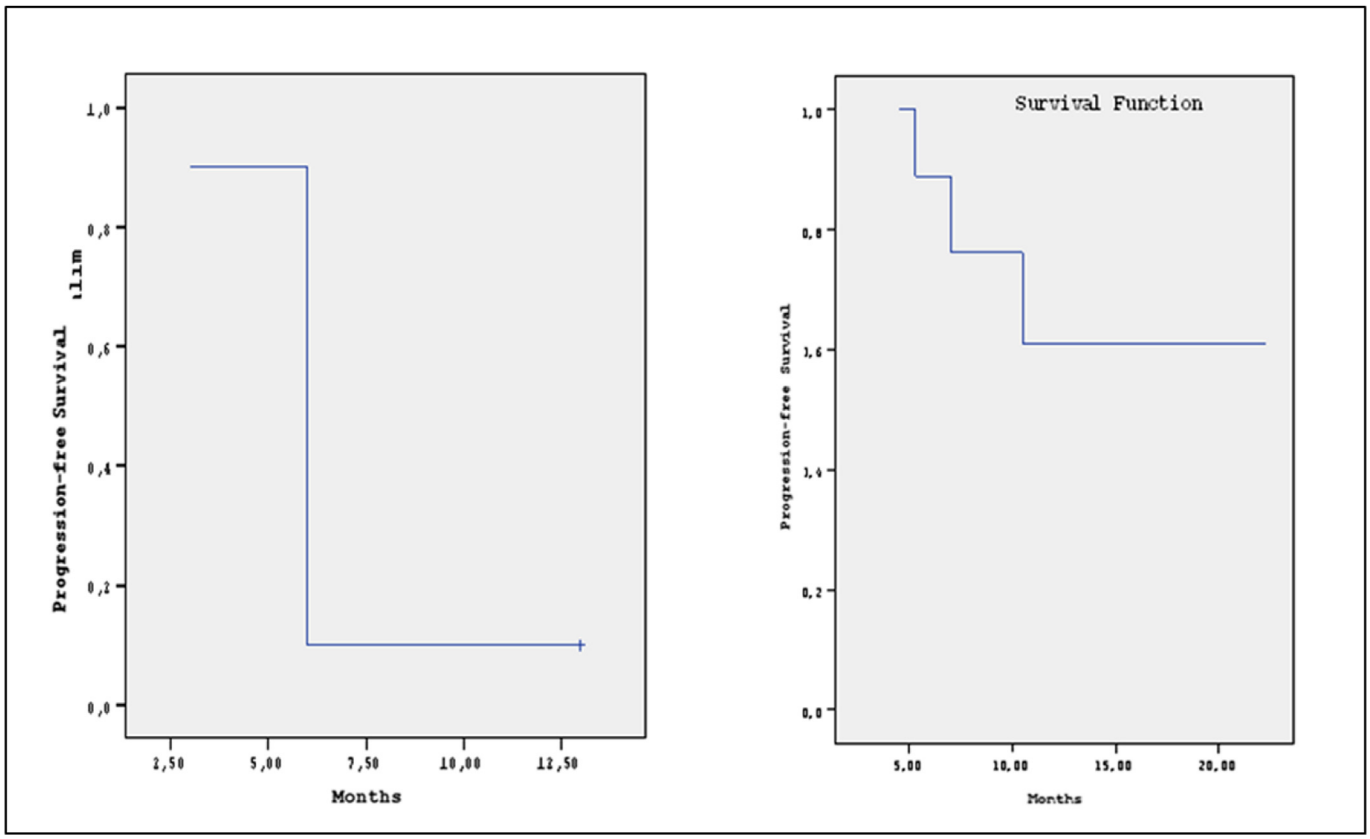

Fig. 1. Progression-free survival and overall survival curves of Brentuximab Vedotin treatment.

Long-term remission cannot be achieved with the conventional treatment options in about 30% of classical HL. The standard treatment approaches for these patients currently are high-dose therapy and autologous bone marrow transplantation (ABMT). BMT provides long-term remission in only 50% of patients.[6]

BV, an antibody-drug conjugate, specifically binds to CD 30 (+) malignant HRS cells and shows tumoricidal effect via a microtubule inhibitor, monomethyl auristatin E (MMAE), that is also structurally built-in.[7] BV - AVD could be an alternative treatment for patients with pulmonary dysfunction in order to avoid the pulmonary adverse effects of bleomycin. Non-infectious pulmonary toxicity including interstitial lung diseases, pneumonitis, and acute respiratory distress syndrome has been reported.[8,9] Nevertheless, the effects and adverse effects of BV have not been specialized on patients with pulmonary involvement.

The International Prognostic Score (IPS) predicts the prognosis of HL patients by the mean of seven prognostic factors. Lymphopenia, which is defined by IPS as less than 600 cells/μL or less than 8% of total white blood cell count have been stated to be associated with poor survival in HL cases.[10] New easier markers are searched. Absolute monocyte count (AMC), absolute lymphocyte count (ALC) and absolute neutrophil count (ANC) had been suggested as significant prognostic factors in HL.[11] In addition neutrophil to lymphocyte ratio (NLR) had been demonstrated to be useful in determining the clinical extent and prognosis in many chronic diseases including HL.[12,13] It has still not been identified whether NLR can be used as a prognostic marker in patients treated with BV or not due to the possible effects of BV on hematological parameters.

We performed this retrospective study considering the lack of data about the outcomes and adverse effects of BV on different extranodal sub-groups of HL and also about the usefulness of NLR in cases treated with BV. We aimed to evaluate the efficacy and toxicity of BV treatment in patients with pulmonary HL in comparison with other HL cases and to demonstrate the role of NLR in patients treated with BV.

2. Material and methods

In this study, data of 10 CD 30 (+) HL patients treated with BV in Medical Oncology Department of Gulhane Health and Education University between August 2011 and January 2016 were analyzed retrospectively. Only the patients treated with BV and relapsed after ABMT or resistant to at least two lines of chemotherapy were included in this study. The study was approved by the local ethics committee of Gulhane School of Medicine. Staging of all patients before BV treatment was performed using PET-CT. Data including the age, gender, age at diagnosis, stage at diagnosis, histopathological type of HL, existence of extranodal involvement, laboratory test results, first-line treatment combination, response to first-line treatment, receiving radiotherapy, time of the first post-treatment relapse, relapse stage, treatment used as salvage therapy, response to salvage treatment, date of ABMT, response to ABMT, date of the post-ABMT recurrence, treatment received after ABMT, stage of the disease before BV treatment, start date, dose, number of cures, response rates and the adverse effects of BV were recorded. The missing data of the patients were completed by contacting the patients.

BV was administered to the patients at a dose of 1.8 mg/kg once every 21 days. Treatment response was assessed at the end of every 3 cycles by FDG PET-CT according to International Working Group response criteria. Toxicity evaluation was performed by the

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