Case Report

Hodgkin Lymphoma Identified After Non-Hodgkin Lymphoma: Two Case Reports

Non Hodgkin Lenfoma Sonrası Tanımlanan Hodgkin Lenfoma: İki Olgu Sunumu

Ersin Bozan, Tuğçe Nur Yiğenoğlu, Mehmet Sinan Dal, Merih Kızıl Çakar, Fevzi Altuntaş

Department of Hematology and Bone Marrow Transplantation Center, Ankara Dr. Abdurrahman Yurtaslan Oncology Training and Research Hospital, University of Health Sciences, Ankara, Turkey

ABSTRACT

The coexistence of different malignant diseases in the same patient is an entity that can rarely be encountered clinically. This can be observed as the presentation of two distinct types of cancer in the same patient simultaneously or at different times. The genetic structure of the individual, environmental factors and chemotherapeutic agents and radiotherapy used in the treatment of primary disease may play a role in this process. Hodgkin lymphoma is hardly ever observed after non-Hodgkin lymphoma treatment. In this report, we aimed to share two cases that were diagnosed with classical Hodgkin lymphoma in their follow-up after non-Hodgkin lymphoma diagnosis and treatment in our clinic.

Keywords: Non-Hodgkin lymphoma, Hodgkin lymphoma, secondary malignancy, relapse

ÖZET

Aynı hastada farklı malign hastalıkların bir arada bulunması klinik olarak nadiren karşılaşılabilen bir durumdur. Bu, aynı hastada aynı anda veya farklı zamanlarda iki farklı kanser türünün ortaya çıkması olarak gözlemlenebilir. Bireyin genetik yapısı, çevresel faktörler, kemoterapötik ajanlar ve birincil hastalığın tedavisinde kullanılan radyoterapi bu süreçte rol oynayabilir. Hodgkin lenfoma, Hodgkin dışı lenfoma tedavisinden sonra neredeyse çok nadir görülür. Bu yazıda, kliniğimizde Hodgkin dışı lenfoma tanı ve tedavisi sonrası klasik Hodgkin lenfoma tanısı alan iki olguyu paylaşmayı amaçladık.

Anahtar Kelimeler: Non-Hodgkin lenfoma, Hodgkin lenfoma, sekonder malignite, relaps

Introduction

The coexistence of different malignant diseases in the same individual is not uncommon in oncology-hematology practice. In the treatment of non-Hodgkin lymphoma (NHL), the risk of secondary malignancy was found to be high in patients who received both radiotherapy and chemotherapy combined therapy [1]. It was observed that NHL before Hodgkin lymphoma(HL) diagnosis were mostly of B-cell origin. While NHL development can be observed after the diagnosis and treatment of HL, the development of HL after NHL diagnosis and treatment is an extremely rare condition. In this report, we discussed two patients who were diagnosed and treated for NHL and later developed HL lymphoma in our clinic. The pathological diagnoses of the patients were

First Received: 13.06.2021, Accepted: 22.11.2021 doi: 10.5505/aot.2022.98470

Table 1. Immunohistochemistry of the biopsies case#1

Markers	NHL Pathology (Initial diagnosis)	HL Pathology
BCL1	Negative	Negative
BCL2	Positive	Negative
BCL6	Positive	Negative
BOB1	Not available	Positive
CD3	Negative	Not available
CD5	Negative	Not available
CD10	Positive	Not available
CD15	Not available	Positive
CD20	Positive	Negative
CD23	Negative	Not available
CD30	Positive	Positive
C-myc	Negative	Positive(weak/dim)
Ki-67	95%	High
LCA	Positive	Negative
MUM1	Positive	Positive
OCT2	Not available	Positive
Pancytokeratine	Negative	Not available
PAX5	Not available	Positive(weak/dim)

BCL: B-Cell Lymphoma, BOB1: B Cell Specific Octamer Binding Protein1, CD: Cluster of Differentiation, LCA: Leukocyte Common Antigen,HL: Hodgkin Lymphoma,MUM1: Multiple Myeloma Oncogene 1, NHL: Non-Hodgkin's Lymphoma, OCT2: Octamer Binding Transcription Factor 2 PAX-5: Paired Box Protein 5.

reconfirmed by re-evaluating the samples. An informed consent form was obtained for both cases.

Case #1

A thirty-eight-year-old male patient applied to the clinic with abdominal pain in January 2018. As a result of the examinations, in the right lung, a mass of 5x5cm in the upper lobe and a mass of 4x5cm in the superior side of the lower lobe was detected on computerized tomography (CT). A 17mm hypodense lesion in the posterior segment of the right liver lobe and thickening of the stomach antrum wall were observed. Upper GIS (gastrointestinal system) endoscopy was performed, malignant ulcer surrounding the lumen infiltrating the pylorus was detected in the distal of the antrum, and the biopsy revealed germinal center diffuse large B-cell lymphoma (DLBCL), the immunophenotype of the biopsy were given in Table 1. Lung biopsy was non-specific and bone marrow biopsy revealed no involvement. The patient was evaluated as Ann Arbor stage 4B DLBCL and R-CHOP (rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate, prednisone) treatment was initiated. After completion of the four-cycle, treatment response was evaluated, the volume of lung masses decreased by 70%, and regarded as (partial remission) PR response. After the treatment was completed with six cycles R-CHOP +2R, control PET-CT was performed. Control PET-CT was compatible as pathological lymph node which size 15x14mm, and SUVmax:13 in the right supra-clavicular region. Prompt biopsy was performed and reported as classical HL. Salvage GDP (gemcitabine, dexamethasone, and cisplatin) treatment was started after the diagnosis of HL. PET-CT was taken to evaluate the response after three cycles of GDP and evaluated as (complete remission)

Table 2. Immunohistochemistry of the biopsies case#2

Markers	NHL Pathology (Initial diagnosis)	HL Pathology
BCL1	Positive (weak/dim)	Negative
BCL 2	Positive	Positive (weak/dim)-rare cells
BCL 6	Positive	Negative
CD3	Negative	Negative
CD5	Negative	Not available
CD10	Negative	Negative
CD15	Not available	Positive
CD20	Positive	Negative
CD23	Positive	Negative
CD30	Negative	Positive
C-myc	Negative	Not available
EBER	Negative	Not available
K.İ.67	99%	High
LCA	Not available	Negative
MUM1	Positive	Positive (weak/dim)- rare cells
PAX5	Not available	Positive (weak/dim)- rare cells

BCL: B-Cell Lymphoma, CD: Cluster of Differentiation, EBER: Epstein Barr Virus Encoded Small RNAs, HL: Hodgkin Lymphoma,LCA:Leukocyte Common Antigen, MUM1: Multiple Myeloma Oncogene 1, NHL:Non-Hodgkin's Lymphoma, PAX-5: Paired Box Protein 5.

CR. After four cycles of GDP, the patient underwent autologous stem cell transplantation (ASCT) with BEAM (BCNU (carmustine), Etoposide, Ara-C (cytarabine), Melphalan) protocol. Brentuximab vedotin (BV) treatment was initiated as maintenance treatment due to the high relapse risk. After the ASCT, the patient under BV treatment was taken PET-CT to evaluate the response at 3rd month and was evaluated as CR.

Case # 2

An eighteen-year-old female patient admitted with shortness of breath, 10 kg weight loss in two months, and night sweats. As a result of the examinations, a 6 cm mass in the anterior mediastinum was detected in thorax CT. Biopsy performed by bronchoscopy was evaluated as a non-germinal center diffuse large B-cell lymphoma, immunophenotype of the biopsy were given in Table 2. The patient was regarded as Ann Arbor stage IV and six cycles R-EPOCH (Rituximab +Etoposide + Prednisone + Vincristine + Cyclo-phosphamide + Doxorubicin) and additional two cycles of rituximab were given. Treatment response evaluation was done after the completion of treatment. Cervical LAP with 4,68 SUVmax (Deauville score:3) was detected and the patient was regarded as refractory. Salvage R-GDP therapy was initiated for two cycles and reevaluation of treatment by the PET-CT response was compatible with CR.The patient underwent ASCT with BEAM protocol in August 2019. In her follow-up, 33x15mm LAP developed in the right supraclavicular region in June 2020. A prompt biopsy was done and reported as classical HL. The pathological diagnoses of the patients were reconfirmed by re-evaluating the same samples. Bendamustine and brentuximab treatment was initiated and now the treatment is ongoing.

Discussion

In this article, two patients who were recently diagnosed HL with after being diagnosed and treated as NHL in our clinic are discussed.

Due to the development of diagnosis and treatment modalities, surveillance after NHL is prolonged and the rate of secondary malignancy increases [2]. Development of HL can be seen in the follow-ups after NHL treatment, though; it is a very rare condition [3-4].

Our first case was thirty-eight years old, and our second case was diagnosed with DLBCL at the age of eighteen. The median age of diagnosis of DLBCL is seventy, both patients are in the AYA age group, and in this age group, NHL is uncommon [5-6]. In our first case, the diagnosis period between DLBCL and HL a was eight months. In our second case, this period is twenty months. Studies have shown that the rate of secondary malignancy increases as the time after diagnosis increases [4].

Patients diagnosed with non-Hodgkin lymphoma have an increased risk of not only Hodgkin lymphoma but also all cancers [4,7-9]. The frequency of non-Hodgkin lymphoma after Hodgkin lymphoma varies between 1-6% [10]. In patients with NHL, the risk of developing HL has increased three times compared to the normal population and the prognosis was found to be worse than de novo HL patients. According to a retrospective study, HL was reported in 14 of 29153 NHL patients [11]. In conclusion, inadequate immune surveillance, exposure to chemo-radiotherapy during treatment, and genetic structure are effective in increasing the risk of lymphoma development and poor prognosis. More clinical studies are needed to fully elucidate this issue.

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Corresponding author e-mail: ersinbozan87@gmail.com

Orcid ID:
Ersin Bozan 0000-0002-3307-3121
Tuğçe Nur Yiğenoğlu 0000-0001-9962-8882
Mehmet Sinan Dal 0000-0002-5994-2735
Merih Kızıl Çakar 0000-0003-0978-0923
Fevzi Altuntaş 0000-0001-6872-3780

Doi: 10.5505/aot.2022.98470

