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Chronic myeloid leukemia following Hodgkin's lymphoma: Case report

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Abstract

Secondary chronic myelocytic leukemia after treatment of Hodgkin's lymphoma is a very rare entity. Here we report a case of an 18 years old male patient who presented at our institution for a right palpable cervical mass without any symptoms. On physical exam, he has fixed, non-tender cervical mass. The biopsy of the cervical mass was in favor of a nodular lymphocyte predominant Hodgkin's lymphoma. He was treated by four cycles of rituximab and 13 sessions of radiotherapy. PET scan showed complete remission with a Deauville score of 1. After 15 months of complete radiotherapy, the patient developed high white blood count 184000, BOM, myelogram and flow cytometry findings are consistent with CML, Fluorescence in Situ Hybridization (FISH) was positive for a BCR-ABL1, and negative for JAK2. Clinically relevant variant were not detected by NGS. Dasatinib 100 mg daily was started.

Keywords: Hodgkin's lymphoma; Chronic myeloid leukemia; Secondary malignancy.

Introduction

According to the World Health Organization (WHO) classification of lymphoid malignancies, Hodgkin's Lymphoma (HL) is divided in 2 groups: classical Hodgkin's Lymphoma (cHL) and Nodular Lymphocyte Predominant Hodgkin's Lymphoma (NLPHL) [1]. NLPHL accounts for 5% of cases and unlike the cHL, lymphocyte-predominant cells express B cell markers (CD20, CD79a, BCL6, etc.) and are negative for CD15 and CD30. Treatment of this entity depends on risk stratification and staging of the disease with options ranging from active surveillance to radiotherapy, anti-CD20 and chemotherapy [2]. Patients with HL face a heightened risk of long-term complications including the development of secondary malignancies. Research indicates that patients treated with both radiotherapy and chemotherapy, are at increased risk of developing secondary cancers. Lung and breast cancers are the most frequently observed solid tumors after Hodgkin's disease treatment and their occurrence is linked to prior radiotherapy, particularly in young females for breast cancer and in old men for lung cancer [3,5]. Secondary Acute Myeloid Leukemia (AML) or Myelodysplasia (MDS) risk is higher in patients treated with intensified chemotherapy protocol (BEACOPP) [6]. However, there are limited reported cases of secondary Chronic Myeloid Leukemia (CML) following HL in the literature. In this paper, we discuss a case of a young patient who developed CML more than one year following the treatment of a NLPHL.

Case presentation

It's a case of an 18-year-old male, previously healthy, who presented to his family medicine institution in September 2021 for a palpable right cervical mass. On physical exam, there was a fix nontender mass in the right cervical area, without surrounding erythema or edema. The patient didn't report any associated symptoms including fever, night sweats or weight loss. Complete blood tests and viral serologies were unremarkable. The biopsy of the cervical mass was in favor of nodular lymphocyte predominant Hodgkin's lymphoma. An FDG-PET CT scan revealed a large markedly avid right cervical mass measuring 5.1 x 4.1 x 7.3 cm seen at the right upper jugular station showing significant FDG avidity with SUV max 28.6. No other suspicious findings were seen. The patient received 4 cycles of Rituximab

375 mg/m^2 weekly, followed by a partial response on PET CT scan with a Deauville score of 4. He underwent radiotherapy on the cervical mass in February 2022 (30 Gray in 15 sessions). In May 2022, at the end of the treatment, PET SCAN showed a complete response with a Deauville score of 1. 15 months after the completion of radiotherapy, a complete blood count on a routine visit showed a hyperleukocytosis (WBC 184000). Hemoglobin and platelets count were normal. No blasts were found on peripheral smear. PET scan showed a persistent complete remission. PCR BCR-ABL was positive and PCR JAK2 was negative. A myelogram, flow cytometry and bone marrow biopsy were also consistent with chronic myeloid leukemia. The karyotype also confirmed the presence of translocation 9,22. Next generation sequencing did not show any actionable or clinically relevant variant. A whole genome sequencing for hereditary cancers was also negative. The patient was started on Dasatinib 100 mg daily.

Discussion

CML constitutes approximately 15% of leukemia cases in adults. While the median age at which the disease typically presents is 67 years, it can manifest in individuals across all age groups [7]. The occurrence of Chronic Myeloid Leukemia (CML) because of a prior treatment is a notably infrequent phenomenon, with limited documentation in medical literature. In addition, the population demographics and cytogenetic profiles of both primary and secondary CML cases frequently display considerable similarity, creating uncertainty about whether reported instances genuinely represent secondary malignancies or arise from spontaneous, de novo mutations [8].

Few cases of secondary CML after lymphoid malignancies are reported in the literature including a patient who developed a secondary CML 10 year after chemotherapy and radiotherapy for the treatment of tonsillar diffuse large B cell lymphoma (DLBCL) [9]. The occurrence of secondary CML after Hodgkin's lymphoma was also described in some cases and the duration between the end of treatment for HL and the development of CML is variable between 5 to 8 years. A case series of 3 patients who developed CML 5 years after HL remission found a rare mutation with BCR-JAK2 fusion in one patient that could be related to the occurrence of CML. The other cases are most likely treatment related especially to radiotherapy [10,11].

In our case, we didn't find any genetic variation that could be related to a predisposition to develop HL or CML. Furthermore, the little timeframe between the two diagnoses raises the hypothesis that CML could be a secondary malignancy related to HL. This patient received Rituximab alone without chemotherapy. In fact, a meta-analysis including patients with NHL treated or not with Rituximab, did not show a significant correlation between Rituximab and the risk to develop secondary cancers [12]. Thus, radiotherapy is probably the main causative factor for the development of CML in this case but the short timeframe between the two diagnoses is against this hypothesis. Sorituximab, it will be the first case in the litterature causing CML. To sum up, based on all the arguments detailed above, this is a rare case of treatment related CML. Other hypotheses remain possible including a genetic and an environmental susceptibility to malignancies or a consequence of immunodeficiency secondary to HL.

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