Complete remission of refractory Hodgkin’s lymphoma in a patient with AIDS after single dose checkpoint inhibitor therapy

Aswanth Reddy, Abigael Luke, Joerg Rathmann

ABSTRACT

Introduction: Hodgkin’s lymphoma (HL) is a hematopoietic neoplasm that arises from the preapoptotic germinal or postgerminal center B cells. It is characterized by the neoplastic Reed–Sternberg cell, of which they are few in number relative to surrounding dense inflammatory infiltrate elicited by the neoplastic B cell. The incidence of HL is higher in patients with human immunodeficiency virus (HIV) and the risk of developing HL increases 10-fold in patients with CD4 cell count <100 cells/mm. Case Report: A 65-year-old man with HIV presented with recurrent classical HL. His initial diagnosis was in 2010 when he was treated with adriamycin, bleomycin, vinblastine, dacarbazine (ABVD) and first recurrence in 2017 when he received brentuximab. At this recurrence, he had extensive disease, poorly controlled HIV, and elevated liver function tests. He was started on nivolumab but after one dose he deteriorated clinically with worsening bilirubin. He was transitioned to best supportive care and when eventually seen in the outpatient clinic he had complete recovery of liver dysfunction which coincided with complete remission of his HL, confirmed by a repeat positron emission tomography/computed tomography (PET/CT).

Conclusion: Nivolumab is currently approved for treatment of relapsed or refractory HL after brentuximab and autologous stem cell transplant. The paucity of data regarding the efficacy of nivolumab in HIV-related HL is attributable in part to the exclusion of HIV positive patients from registration trials. We conclude that immune checkpoint inhibitor therapy should be considered for patients with HIV-related HL if they are transplant ineligible, irrespective of their CD4 count and tumor burden.

Keywords: CD4, Hodgkin’s, Human immunodeficiency virus, Nivolumab

INTRODUCTION

Hodgkin’s lymphoma (HL) is a hematopoietic neoplasm that arises from the preapoptotic germinal or postgerminal center B cells. It is characterized by the neoplastic Reed–Sternberg cell, of which they are few in number relative to surrounding dense inflammatory infiltrate elicited by the neoplastic B cell. The two major subtypes include the classical type and nodular lymphocyte predominant type. In 2017, there were estimated to have been 8260 new cases of HL and about 1070 reported deaths in the United States [1]. Hodgkin’s...
lymphoma has a bimodal age distribution and peaks at the ages of 20 and 65. The incidence of HL is higher in patients with HIV, and almost all HL patients show positivity for Epstein–Barr virus. The risk of developing HL increases 10-fold in patients with CD4 cell count <100 cells/mm³, and the incidence increases during the first three months following initiation of antiretroviral therapy [2]. The remarkable discovery of chromosome 9p24.1 amplification, leading to increased expression of programmed cell death protein 1 (PD-1) ligand in HL, has led to the use of immune checkpoint inhibitor therapy for HL [3]. Nivolumab and pembrolizumab have shown favorable treatment responses and are food and drug administration (FDA) approved for relapsed or refractory disease.

CASE REPORT

A 65-year-old man with HIV on highly active antiretroviral therapy (HAART) presented with recurrent classical Hodgkin lymphoma (cHL) and visceral crisis. His initial diagnosis was in 2010 when he was treated with 6 cycles of adriamycin, bleomycin, vinblastine, dacarbazine (ABVD) achieving complete remission. The first recurrence was in 2017 when he had extensive lymphadenopathy, splenomegaly, and innumerable osseous lesions. He received 6 cycles of brentuximab, achieving a near-complete remission by April 2018. He subsequently presented in July 2018 with extensive disease relapse, confirmed by excisional lymph node biopsy, and marrow exam documenting 80% replacement of bone marrow by cHL. A PET/CT imaging showed marked progression at multiple sites (Figure 1). At that time, total bilirubin was elevated at 13.3 mg/dL, and alkaline phosphatase of 1142 U/L. His CD4 count was 53 cells/uL. He was treated with nivolumab, receiving only a single dose of 240 mg. However, he was readmitted to the hospital one week later due to significant clinical deterioration, pancytopenia, and progressively worsening liver failure. The total bilirubin escalated to 15.6 mg/dL. He was treated with steroids for possible nivolumab-induced liver injury, and discharged home after a prolonged hospital stay, with hospice care recommended. However, he recovered slowly, without further treatment of HL, and on follow-up after eight weeks he had completely recovered liver function (Table 1). A restaging PET/CT imaging showed a complete response without any evidence of disease (Figure 2). The bone marrow exam was repeated and showed no residual HL. His CD4 count continues to be low at 98 cells/uL, and he is continuing HAART therapy. He is followed closely

Table 1: Timeline of laboratory values during hospitalization for relapsed disease

<table>
<thead>
<tr>
<th>Month</th>
<th>Total bilirubin (mg/dL)</th>
<th>Direct bilirubin (mg/dL)</th>
<th>Alanine aminotransferase (U/L)</th>
<th>Aspartate aminotransferase (U/L)</th>
<th>Alkaline phosphatase (U/L)</th>
<th>Lactate dehydrogenase (U/L)</th>
</tr>
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<tbody>
<tr>
<td>June 2018</td>
<td>0.6</td>
<td>0.2</td>
<td>8</td>
<td>12</td>
<td>371</td>
<td>163</td>
</tr>
<tr>
<td>July 2018</td>
<td>13.3</td>
<td>9.6</td>
<td>75</td>
<td>104</td>
<td>1142</td>
<td>763</td>
</tr>
<tr>
<td>(Hospital admission)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>July 2018</td>
<td>15.6</td>
<td>9.6</td>
<td>70</td>
<td>90</td>
<td>867</td>
<td>188</td>
</tr>
<tr>
<td>(After nivolumab)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>October 2018</td>
<td>1.1</td>
<td>NA</td>
<td>45</td>
<td>44</td>
<td>846</td>
<td>158</td>
</tr>
</tbody>
</table>

Figure 1: PET/CT at disease recurrence showing extensive fluorodeoxyglucose (FDG) activity in bone, liver, spleen, and lymph nodes involving hilar, mediastinal, and retroperitoneal regions.

Figure 2: PET/CT after one dose of checkpoint inhibitor therapy showing no FDG activity confirming a complete remission.
and the plan is to resume checkpoint inhibitor therapy at disease recurrence.

DISCUSSION

Nivolumab is currently approved for treatment of relapsed or refractory HL after brentuximab and autologous stem cell transplant. In our patient, we used nivolumab as third-line therapy as he was not a candidate for transplant due to poor performance status, liver dysfunction, and extent of disease. A literature search revealed only two cases of HIV-related HL who had a favorable response to PD1 inhibitor. Chang et al. reported a HIV patient with refractory HL who was treated with nivolumab after three lines of prior cytotoxic chemotherapy and the patient achieved a remission after 8 cycles of nivolumab [4]. The CD4 counts of this patient were 391 and 426 cells/mm³ at the start and end of therapy, respectively. Sandoval-Sus et al. reported a HIV patient with refractory HL and extensive liver involvement who had four prior lines of treatment [5]. This patient was treated with nivolumab as fifth-line treatment and had a remission with resolution of liver dysfunction after 10 treatments. CD4 counts were 103 and 126 cells/mm³ before and after treatment for this patient. Each of these patients mentioned above had multiple doses of PD1 inhibitor therapy, as compared to our patient who received only a single dose of nivolumab. The paucity of data regarding the efficacy of nivolumab in HIV related HL is attributable in part to the exclusion of HIV positive patients from registration trials.

CONCLUSION

We conclude that immune checkpoint inhibitor therapy should be considered for patients with HIV-related HL if they are transplant ineligible, irrespective of their CD4 count and tumor burden.

REFERENCES


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Author Contributions

Aswanth Reddy – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Abigail Luke – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Joerg Rathmann – Conception of the work, Design of the work, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Guarantor of Submission

The corresponding author is the guarantor of submission.

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None.

Consent Statement

Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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