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Promising effect of PDL1 inhibitors in the front-line management of primary aggressive central nervous system lymphoma: A case report

Rasha El-Tawab
Department of Hematology, Kuwait Cancer Control Center, Kuwait

Abdulaziz Hamada
Department of Hematology, Kuwait Cancer Control Center, Kuwait

Rehab Elhagracy
Department of Hematology, Kuwait Cancer Control Center, Kuwait

Karen Pinto
Department of Pathology, Kuwait Cancer Control Center, Kuwait

Salem Alshemmari
Department of Hematology, Kuwait Cancer Control Center, Kuwait, salem@hsc.edu.kw

CASE REPORT

Promising Effect of PDL1 Inhibitors in the Front-Line Management of Primary Aggressive Central Nervous System Lymphoma: A Case Report

Rasha El-Tawab [a], Abdulaziz Hamada [a], Rehab Elhagracy [a], Karen Pinto [b], Salem Alshemmari [a,*]

[a] Department of Hematology, Kuwait Cancer Control Center, Kuwait
[b] Department of Pathology, Kuwait Cancer Control Center, Kuwait

Abstract

Primary central nervous system lymphoma (PCNSL) is a rare lymphoma that involves the central nervous system. The standard treatment involves chemotherapy with high-dose methotrexate. To the best of our knowledge, this is the first reported case of employing checkpoint inhibitor, nivolumab, alone to treat a patient with PCNSL who could not tolerate the induction therapy. In aggressive cases of PCNSL where chemotherapy may become futile, stand-alone checkpoint inhibitors should be considered as the front-line treatment protocol.

Keywords: Immunotherapy, Primary CNS lymphoma, Checkpoint inhibitor

1. Introduction

Primary central nervous system lymphoma (PCNSL) is a rare and aggressive extranodal non-Hodgkin lymphoma. The median overall survival of patients with PCNSL is <50 months, with recurrence rates of almost 50% within the first 2 years of diagnosis [1,2]. Nivolumab is an immune checkpoint inhibitor that targets programmed cell death-1 (PD1) receptors and blocks its interaction with programmed death-ligand 1 (PDL1) and 2 (PDL2). The PD1 receptor is a negative regulator of T-cell activity that is involved in the control of T-cell immune response [3].

We report a patient with PCNSL who could not tolerate the induction therapy with methotrexate (MTX) and cytosine arabinoside (Ara-C). The patient had a very poor performance status Eastern Cooperative Group scale (ECOG 4) attributed to progressive diffuse large B-cell lymphoma. His condition resulted in respiratory failure requiring ventilatory support. His ICU course was complicated with recurrent episodes of sepsis. The repeat magnetic resonance imaging (MRI) after the first dose of MTX and Ara-C revealed progressive disease. The treating physician believed that further chemotherapy would be deleterious to his already poor general condition.

The patient was started on single-agent nivolumab 3 mg/kg every 2 weeks. Impressive clinical response was observed in this patient after just four doses of nivolumab. In particular, significant rapid clinical improvement was obtained despite his poor performance status. The patient became mobile and self-dependent within 4 months with one-sided residual motor weakness after eight doses.

2. Case presentation

The patient, a 36-year-old man, was initially labeled to have demyelinating disease and was given short courses of prednisone. His symptoms

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* Corresponding author at: Department of Medicine, Faculty of Medicine Kuwait University PO BOX 24923-13110 SAFAT Kuwait. Tel.: 00965-25319596.
E-mail addresses: dr.karenpinto@gmail.com (K. Pinto), salem@hsc.edu.kw (S. Alshemmari).

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improved on prednisone but later became worse, with obvious one-sided motor weakness and decreased cognitive functions. The baseline computed tomography scan of the brain on October 16, 2017, showed evidence of multiple enhancing intra-axial focal lesions seen in the right cerebellar hemisphere and occipital lobe as well in the left temporal lobe in the parasagittal location, with associated mild perifocal edema, causing mild effacement of the third and fourth ventricles with subsequent asymmetrical dilatation of the right lateral ventricle. The largest lesion was seen in the right occipital lobe measuring 2.3 × 2.7 cm Fig. 1.

Brain biopsy which showed diffuse large B-cell lymphoma of non-germinal center B-cell like and chronic meningoencephalitis Ki67 measured at 35% and the examined tissue tested positive for CD20, PAX5, CD5, BCL-2, BCL-6, and MUM-1. There was no expression of C-MYC1 noted in the examined tissue. Dural biopsy and blood vessel showed no significant pathology.

The patient was initiated on the following treatment combination: rituximab 375 mg/m^2, on day 1, MTX 3.5 g/m^2, a total dose of 7 g and cytarabine 2 g/m^2 every 12 h, a total dose of 4 g on day 2. Despite the timely initiation therapy, the patient's condition deteriorated rather rapidly perhaps as a result of disease progression. Consequently, the patient became comatose requiring artificial ventilation to protect his airways. The repeat brain imaging documented disease progression, with no signs of intracranial hemorrhage.

Given the grief circumstances, further chemotherapy was regarded to be futile and contraindicated. As PDL1 expression is well known in PCNSL cases, we started checkpoint inhibitor, nivolumab, at a dose of 3 mg/kg every 2 weeks. Following six cycles of nivolumab, his general condition demonstrated remarkable improvement. He regained his level of consciousness. This allowed faster weaning off the ventilatory support. Fig. 2 shows the MRI study after six cycles of treatment with checkpoint inhibitor, with almost complete resolution of his brain lesions Fig. 2.

The patient was discharged in June 2018 to the rehabilitation center for further active physiotherapy. He continued to be on nivolumab at the current dose of 3 mg/kg, of which he received a total of 16 cycles, the last being in February 2019. He continues to be in complete remission. No side effects have been documented so far.

3. Discussion

Primary testicular lymphoma and PCNSL are rare and aggressive extranodal non-Hodgkin lymphomas with shared molecular features and poor prognosis. PCNSLs arise from the brain, spinal cord, leptomeninges, or eye in the absence of prior or concurrent systemic disease. The median overall survival of patients with PCNSL is 30–50 months, with recurrence rates of almost 50% within the first 2 years of diagnosis.

This case demonstrates the powerful effect of checkpoint inhibitors in the management of patients with PCNSL. High PDL1 expression is well documented among patients with PCNSL [4]. In our center, young patients with PCNSL are typically treated with high-dose chemotherapy (HDC) and peripheral blood stem cells rescue in accordance with the MATRix regimen [5]. However, the poor clinical performance of this patient did not allow for

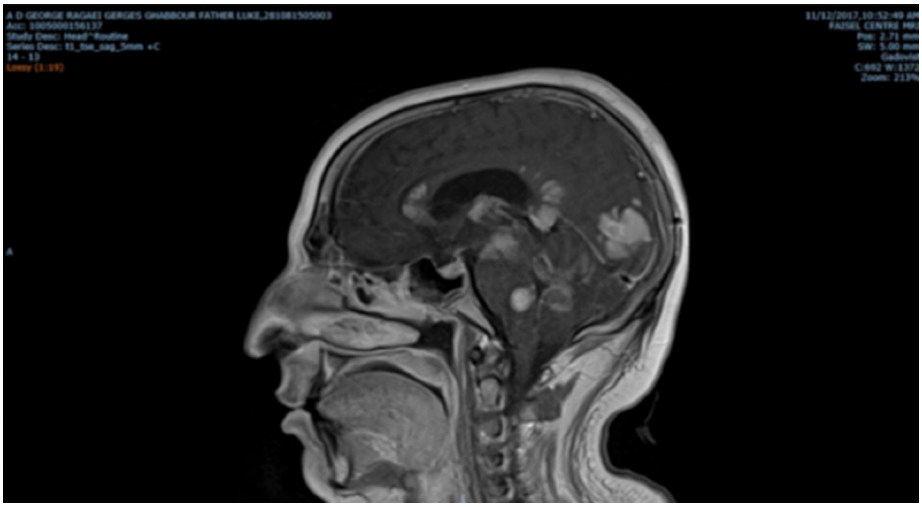

Fig. 1. Lymphoma at the posterior occipital site.

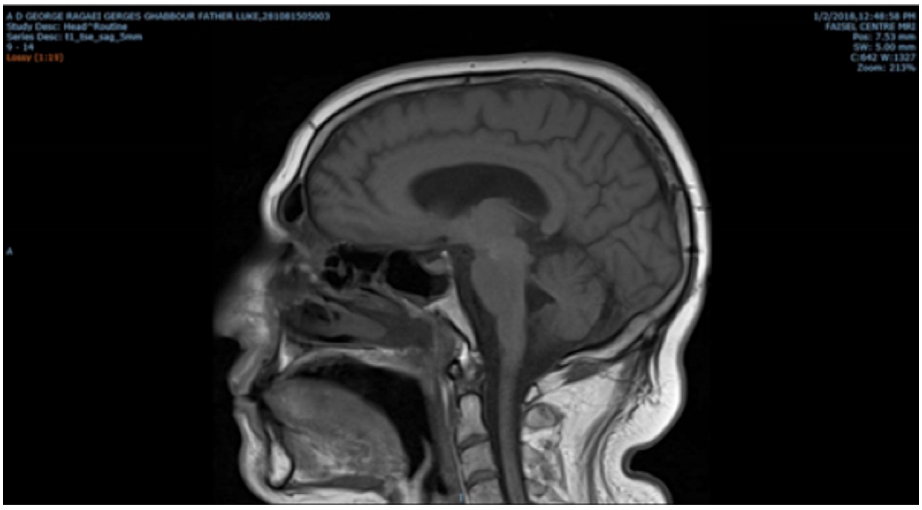

Fig. 2. Total resolution of all the lesions after six cycles of treatment with checkpoint inhibitor.

what we consider the standard of care at the time of his presentation. Furthermore, radiotherapy alone in PCNSL has suboptimal outcome and many serious complications.

There are few case reports in the literature that demonstrated the feasibility of checkpoint inhibitors among relapsed refractory PCNSL [4]. To our knowledge, no cases have been reported with checkpoint inhibitors alone for the treatment of aggressive PCNSL.

As the patient has achieved complete response and his general condition has improved, what would be the next approach to such a case? We elected to continue the immunotherapy approach for the time being. Our planned strategy for salvage, if relapse does occur in the future, is combination chemoimmunotherapy and HDC with autologous peripheral blood rescue.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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