Annals of Short Reports and Clinical Images

Case Report

Selinexor in the Treatment of a Patient with Refractory Plasmablastic Lymphoma: A Case Reports

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Abstract

Plasmablastic lymphoma (PBL) is an uncommon and aggressive subtype of diffuse large B-cell lymphoma that commonly associated with HIV infection. However, PBL can also occur in patients with other immunodeficiencies diseases or in immunocompetent individuals. The HIV-negative PBL usually has a worse prognosis than that in HIV-positive patients. The median OS of plasmablastic lymphoma patients with HIV infection is 15 ~ 17 months after treatment, while the median OS of PBL patients with HIV negative is only about 9 months. The treatment of PBL is quite challenging, and currently there is no standard of therapy for this entity. Therefore, new approaches of novel medications are needed to improve its poor prognosis. Selinexor is a novel selective nuclear export inhibitor which selectively binds to export protein 1 (XPO1), leading to cell cycle arrest and apoptosis. In this case, we had achieved a rapid and significant response under treatment of selinexor combined with chemotherapy in a heavily pretreated HIV-negative plasmablastic lymphoma young patient with multiple extranodal infiltration. It is reported as follows.

Introduction

Plasmablastic lymphoma is a distinct lymphoma that is generally associated with immunosuppression patients [1-4]. An extranodal presentation involving the oral cavity is the most common in the setting of uncontrolled HIV infection PBL [5]. However, PBL in immunocompetent individuals seems to be more heterogeneous in terms of sites of involvement, such as gastrointestinal, skin, bone and nose [3]. PBL has an aggressive clinical outcome with an overall survival 6–12 months [6]. The selective inhibitor of exportin 1 (XPO1) selinexor has been approved by FDA for the treatment of diffuse large B-cell lymphoma (RR DLBCL) and relapsed or Refractory Multiple Myeloma (RR MM) which has a remarkable therapeutic effect [7,8]. Here we report a case that showed a profound response to selinexor in an HIV-negative, EBV-negative heavily pretreated PBL young patient.

Case Presentation

The patient was a 25-year-old Chinese male who presented with bloody nasal mucus and swelling nasal area went to a local hospital in January 2021. Initially it was considered as a sinusitis. The patient had a surgery of sinus fenestration, nasal septum submucosal resection and sinus lesion resection under nasal endoscopy on 6th March 2021. Postoperative pathology showed blastic/plasmablastic features, indicating of plasmablastic lymphoma. Extensive immunohistochemical staining was performed showing that neoplastic cells expressed a plasma cell phenotype with CD138+, Lambda+, VS38c partially+, while CD20-, CyclinD1-, CD3-, CD79a-, CD56-, CD30-, EMA-, kappa-, Desmin-, HMB45-, Syn-, S100- are all negative. A proliferative index Ki67 was 60% positive. Lab tests of hemoglobin, hematocrit, and serum calcium, β2-microglobulin, LDH levels were all within the normal reference ranges. Hepatitis B virus, Epstein-Barr Virus DNA, and HIV were all negative. There was no evidence of lymphoma involvement in bone marrow. The whole-body PET-CT scan demonstrated that the left maxillary sinus, left ethmoid sinus soft tissue, bilateral submandibular lymph nodes, and nodules on the 3rd and 8th thoracic vertebrae located in the lower left posterior mediastinum area increased FDG metabolism, consistent with lymphoma manifestations. The Ann Arbor staging II, an Eastern Cooperative Oncology Group (ECOG) performance status of 1, and the international Prognostic Index (IPI) score of 0. The patient started with 2 cycles of Bortezomib-CHOP (cyclophosphamide, adriamycin, vincristine, prednisone) chemotherapy every 4 weeks. After the second cycle of treatment, he experienced a new left infraorbital mass which gradually increased, and MRI confirmed disease progressed (PD). Then the patient changed to received Bortezomib combined with hyper-CVAD regimen (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) in one cycle on 5th July. During this treatment the left infraorbital mass began to shrink on MRI image. Radiotherapy started for the left maxillary sinus, ethmoid sinus, and cervical lymph nodes on 13th July. During radiotherapy disease progression was seen, clinically manifested as cervical and axillary lymph nodes enlarged. The patient was salvaged with Bortezomib-CHOP chemotherapy regimen on 27th July. The autologous blood stem cell collection was performed on 11th August. The patient had a PET-CT scan second time on 23rd August (Figure 1A), confirmed that the left maxillary sinus and ethmoid sinus, and the thickened left inferior turbinate mucosa decreased FDG metabolism activity compared with those in previous image; Nonetheless, the bilateral posterior cervical triangle, bilateral axilla, anterior mediastinum, posterior mediastinum, Aortopulmonary Window (APW), left anterior diaphragm group, bilateral diaphragmatic crura posterior, bilateral adrenal gland area, gastric minor curvature, retroperitoneum around abdominal aorta,

Citation: Yuhua F, Renjun B, Yonghua Y, Zhang T, Chen L. Selinexor in the Treatment of a Patient with Refractory Plasmablastic Lymphoma: A Case Reports. Ann Short Rep Clin Image. 2022; 3(3): 1028.

Publisher Name: Medtext Publications LLC

Manuscript compiled: Apr 07th, 2022

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posterior and lower right kidney, right paracolic sulcus, greater curvature of the gastric body, subcutaneous body, left psoas major, right thigh muscles, left ninth rib, right ilium, left ischia, those bone's FDG metabolism increased notably. It is considered lymphoma multi-system involvement, and disease Progressed Diffusely (PD).

Under these medical conditions, the patient received a novel, oral selective inhibitor of nuclear export-1 (SINE) selinexor on 27th August. Selinexor was started at a dose of 60mg on days 1, 8, 15, with GDP (gemcitabine, cisplatin, dexamethasone) regimen every 3 weeks. Remarkably, in the first two weeks selinexor was enough to induce a drastic clinical improvement. On 13th Sep, the whole-body PET-CT showed that both sides of the deep superior cervical space, right axilla, main aortopulmonary window, left anterior diaphragm group, left diaphragmatic crura posterior, left adrenal area, gastric minor curvature, retroperitoneum around the abdominal aorta, left 9th rib, right ilium and left ischia, those multiple bones, and bilateral pleural lesions were significantly reduced FDG metabolism (Figure 1B). Besides, multiple nodules' size in subcutaneous soft tissue decreased after first cycle treatment. The therapeutic effect of selinexor combination regimen was evaluated as Partial Response (PR). He was able to receive ASCT on Sep 24th followed selinexor maintenance until now. As of this writing, this patient continued in response for 2 cycles of Selinexor treatment. Patient were administered anti-nausea medication palonosetron hydrochloride prior to and during treatment with selinexor. The adverse events were leukopenia 2.38×10^9/L (Grade 2) with normal neutrophils, erythropenia 4.03×10^{12}/L (Grade 1), the thrombocytes and other lab results were all within normal limits. All AEs were mild, expected, and manageable with appropriate supportive care.

Discussion

Plasmablastic Lymphoma (PBL) is a very rare malignancy with distinct clinicopathologic characteristics and high recurrence and mortality rate. Though PBL is mostly diagnosed in Human Immunodeficiency Viruses (HIV)-positive patients, it turns out that HIV-negative PBL displays a higher degree of chemoresistance, shortened survival rate when compared to those in HIV-positive PBL [9]. Currently, there is no standard treatment of PBL, the most common treatment options are mainly chemotherapy based on CHOP regimens, radiotherapy and Autologous Hematopoietic Stem Cell Transplantation (ASCT). However, the existing treatments have quite short remission periods. It is urgent to explore new medications to seek better efficacy and longer survival. In view of the similarities between the immunophenotypes of PBL and multiple myeloma, some scholars have applied Bortezomib and thalidomide to the treatment of PBL, but the long-term effect is not good [10]. In our case, despite of administering multiple lines of proteasome inhibitor combined with chemotherapy and radiation therapy, this patient's disease continued to progress. Therefore, we tried to apply a new mechanism drug of XPO1 inhibitor selinexor. Selinexor is a novel, oral, first-in-class Selective Inhibitor of Nuclear Export (SINE) compound which uniquely targets exportin-1(XPO1). In preclinical studies, it has been proved that selinexor can cause intracellular storage and reactivation of many tumor suppressor proteins (eg, p53, IkBκ, RB1, p27, FOXO) and other growth regulatory proteins. Meanwhile, selinexor has the capacity of down-regulate a variety of carcinogenic proteins, thus blocking cell division cycle, inducing apoptosis of a large number of solid and blood tumor cells in vitro and in vivo. In preclinical studies, it has been reported that selinexor has a synergistic effect in combination with GDP chemotherapy, which is considered to be related to the mechanism of inhibiting FOXO1 nuclear export and inducing p27 active, reducing survivin levels and inhibiting the accumulation of DNA repair proteins [11,12]. To the best of our knowledge, this is the first reported case of plasmablastic lymphoma under selinexor treatment. This patient had heavily prior exposure to proteasome inhibitor, chemotherapy and radiation therapy. However,

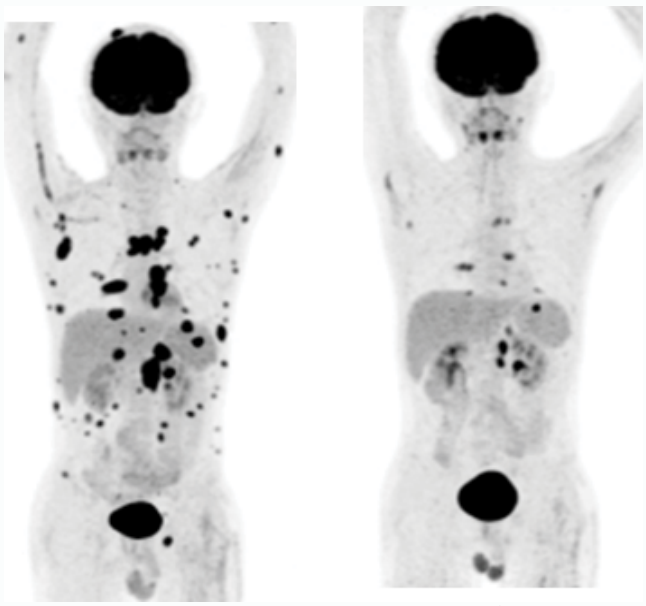

Figure 1: A) The patient's whole-body PET-CT image before the selinexor+GDP regimen showed that the lymphoma was involved in multiple systems.
B) The patient's whole-body PET-CT image after first cycle of selinexor+GDP regimen showed that the lesions were significantly reduced, FDG metabolism was reduced, and the therapeutic efficacy was evaluated for PR.

Partial Response (PR) to selinexor were seen rapidly as soon as two weeks treatment. Meanwhile, we found that selinexor is safe and tolerable. The most common adverse reactions in this patient were mild hemocytopenia, without nausea, vomiting, or hyponatremia. Selinexor treatment provided a valuable opportunity for this patient to undergo autologous transplantation and brings new hope for the treatment of plasmablastic lymphoma.

In summary, the rapidity and depth of the response to selinexor in this PBL case indicated the promising role of this drug, potentially offering a new therapeutic option for heavily pretreated PBL patients.

References

1. Lopez A, Abrisqueta P. Plasmablastic lymphoma: current perspectives. Blood Lymphat Cancer. 2018;8:63-70.
2. Rodrigues-Fernandes CI, de Souza LL, Santos-Costa SFD, Silva AMB, Pontes HAR, Lopes MA, et al. Clinicopathological analysis of oral plasmablastic lymphoma: A systematic review. J Oral Pathol Med. 2018;47(10):915-22.
3. Castillo JJ, Bibas M, Miranda RN. The biology and treatment of plasmablastic lympho-ma. Blood. 2015;125(15):2323-30.
4. Parikh K, Cang S, Sekhri A, Liu D. Selective inhibitors of nuclear export (SINE)--a novel class of anti-cancer agents. J Hematol Oncol. 2014;7:78.
5. Sarode SC, Sarode GS, Patil A. Plasmablastic lymphoma of the oral cavity: a review. Oral Oncol. 2010;46(3):146-53.
6. Morscio J, Dierickx D, Nijs J, Verhoef G, Bittoun E, Vanoeteren X, et al. Clinicopathologic comparison of plasmablastic lymphoma in HIV-positive, immunocompetent, and post-transplant patients: single-center series of 25 cases and meta-analysis of 277 reported cases. Am J Surg Pathol. 2014;38(7):875-86.
7. Kasamon YL, Price LSL, Okusanya OO, Richardson NC, Li RJ, Ma L, et al. FDA Approval Summary: Selinexor for Relapsed or Refractory Diffuse Large B-Cell Lymphoma. Oncologist. 2021;26(10):879-86.
8. Podar K, Shah J, Chari A, Richardson PG, Jagannath S. Selinexor for the treatment of multiple myeloma. Expert Opin Pharmacother. 2020;21(4):399-408.
9. Castillo JJ, Winer ES, Stachurski D, Perez K, Jabbour M, Milani C, et al. Clinical and pathological differences between human immunodeficiency virus-positive and human immunodeficiency virus-negative patients with plasmablastic lymphoma. Leuk Lymphoma. 2010;51(11):2047-53.
10. Guerrero-Garcia TA, Mogollon RJ, Castillo JJ. Bortezomib in plasmablastic lymphoma: A glimpse of hope for a hard-to-treat disease. Leuk Res. 2017;62:12-6.
11. Azizian NG, Li Y. XPO1-dependent nuclear export as a target for cancer therapy. J Hematol Oncol. 2020;13(1):61.
12. Wang AY, Liu H. The past, present, and future of CRM1/XPO1 inhibitors. Stem Cell Investig. 2019;6:6.