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Autologous stem cell transplant for relapsed peripheral T-cell lymphoma in a dialysis-dependent patient

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Abstract

Many reports of Autologous Stem Cell Transplant (ASCT) in patients with multiple myeloma are available in the literature to determine safety for patients with hemodialysis-dependent End-Stage Renal Disease (ESRD). However, very few report the safety of high-dose chemotherapy followed by ASCT in the context of lymphoma. Here, we present the case of a young patient with ESRD dialysis-dependent that safely underwent ASCT with adjusted single-dose etoposide/melphalan for relapsed Peripheral T-Cell Lymphoma (PTCL) after undergoing Gemcitabine, Dexamethasone, and cisplatin salvage regimen (GDP). He remains in complete remission after 6 months of follow-up.

Keywords: Autologous stem cell transplant; Non-hodgkin lymphoma; Conditioning regimen; T-cell lymphoma.

Introduction

Patients with relapsed peripheral T-cell lymphoma carry a well-known poor prognosis. In the absence of transplant, reported median overall survival is estimated to be approximately 6 months [1]. Although prospective trials are lacking, a systematic review suggests a benefit to a salvage therapy followed by ASCT, with a pooled 1-to-5-year OS of 47% in the relapsed /refractory setting [2]. This treatment approach has been incorporated in expert consensus and major guidelines as standard of care for transplant-eligible patients, as it may be the only treatment option with curative intent [3]. The efficacy varies with PTCL subtype and eligibility should be made based on a risk-benefit assessment.

Although some studies are available to demonstrate safety and efficacy of ASCT with dialysis patients in the context of multiple myeloma [4], only a few cases have been reported in the context of NHL[5-7]. To our knowledge, no case of T-cell lymphoma has been reported so far.

Case Presentation

A 29-year-old male from Haiti presented with Hemophagocytic Lymphohistiocytosis (HLH) in August 2020 for which the underlying cause was found to be a Peripheral T-Cell Lymphoma Not-Otherwise Specified (PTCL-NOS) with a negative CD30, and high expression of Ki67 (>80%). Serologic testing for HTLV-1/2 were negative. On initial diagnosis, he had soft tissue involvement and elevated LDH, but no bone marrow involvement, conferring Prognostic Index for PTCL (PIT) score of 2.

He presented with severe acute kidney injury and renal biopsy revealed collapsing glomerulonephritis for which he required hemodialysis. He achieved complete metabolic response after initial treatment of 6 cycles of CHOEP (cyclophosphamide, doxorubicine, vincristine, etoposide and prednisone). Despite lymphoma remission, his kidney function never recovered, and requires long-term hemodialysis. His case was presented in a tumor board and no ASCT was planned in CR1 given his kidney disease. Unfortunately, during routine follow-up, he was found to have a progressive asymptomatic soft tissue mass, and a biopsy confirmed relapse 16 months later. He received 3 cycles of GDP (Gemcitabine, Dexamethasone, and Cisplatin), and achieved second complete remission on his end-of-treatment PET scan. Peripheral stem cell collection was performed following mobilisation with high-dose cyclophosphamide and filgrastim.

Given his comorbidities, he was deemed ineligible to allogeneic stem cell transplant. Although a high risk of Treatment-Related Mortality (TRM) could be predicted for this patient, he consented to ASTC as a curative intent. Organ evaluation revealed normal cardiac function, asymptomatic decrease in Diffusion Capacity for Carbon Monoxide (DLCO) at 73% of predicted upon pulmonary testing. In addition to his end-stage renal disease, his Hematopoietic Cell Transplantation-Specific Comorbidity Index (HCT-CI) score was 4. Prior to his admission for transplant, his medication consisted of, amlodipine, furosemide, pregabalin, sevelamer and darbepoietin alfa. Infectious work-up revealed latent TB, for which he received isoniazid and prior hepatitis B infection, for which he was prophylactically treated with entecavir. In addition, the patient also had positive serologies for Varicella-Zoster Virus (VZV), and Herpes Simplex Virus (HSV) for which he received prophylactic valacyclovir. Cytomegalovirus (CMV) serologies were positive. Serologies for Human Immunodeficiency Virus (HIV), Hepatitis C Virus (HCV) and Strongyloides stercoralis were negative. Pneumocistic Jirovecii (PJP) prophylaxis with trimethoprim-sulfamethoxazole was given prior transplant and planned to resume after engraftment. No prophylactic antibiotic or anti-fungal were given.

Patient was admitted on November 3rd, 2022 for ASCT. Etoposide 36 mg/m^2 was received on day 4, and melphalan 126 mg/m^2 was given on the following day. An administrative COVID19 test proved positive the day prior stem cell infusion. Although the patient was previously vaccinated, and was completely asymptomatic, he received Tixagevimab and cilgavimab (Evushield) 600 mg, and remdesivir was administered for three days to prevent any complications from the conditioning regimen he had already received. Stem cells dose of 7.86 x 10 x 10^6 CD34/kg were infused as planned on day 0. Dialysis was maintained during his hospital stay. In addition to nosocomial COVID19 infection, he developed grade 2 colitis and uncomplicated febrile neutropenia on day +2 for which he required wide-spectrum antibiotics that were stopped upon engraftment. Neutrophil engraftment occurred on day +10, with filgrastim administration. Additio-

nally, the patient received two packed red blood cell and two platelet transfusions. Last platelet transfusion occurred on day +10 and maintained platelet count >20 x 10^9/L meeting ASCTC platelet recovery definition by day +16. Patient was safely discharged on day +13 with continuous supportive care as outpatient.

Conditioning regimen selection

Given the high risk of a second relapse for PTCL, we considered ASCT consolidation in CR2 for this young patient. Many different conditioning regimens have been described [8], BEAM being mostly used in this condition. In the absence of dose adjustment recommendations for carmustine, predominantly excreted by the kidney and not dialyzable, the risk-benefit balance was deemed unfavorable, and an alternative conditioning regimen was sought. Single-dose etoposide-melphalan regimen has been studied in relapsed Hodgkin lymphoma [9-11] and transformed indolent lymphoma [12] with three year-PFS of approximately 40% and Treatment-Related Mortality (TRM) from 0% to 10% in the previously stated studies. Given that literature supports the use of both molecules in hemodialysis and dose-adjustment recommendations are available in this context, we opted for etoposide-melphalan regimen. Furthermore, both molecules are not dialyzable, allowing for administration without concern for timing of dialysis sessions. Its limited toxicity compared to BEAM or Benda-EAM also favored this regimen. Various references were consulted for renal adjustment [13,14]. Etoposide dose was reduced by 40% (36 mg/m^2 on day-4) and melphalan dose was reduced by 30% (126 mg/m^2 on d-3).

Follow-up

We currently are 6 months after transplant and the patient remains in remission, and on continued dialysis. If the patient faces an unfortunate relapse, several newer agents are available for relapsed and refractory PTCL such as pralatrexate, brentuximab vedotin, and Histone Deacetylase (HDAC) inhibitors, in addition to single agent chemotherapy, but these treatments are typically reserved for palliative intent [3].

Conclusion

This case report illustrates feasibility of dose-adjusted chemotherapy followed by ASCT in the context of relapsed T-cell lymphoma for a patient with dialysis-dependent ESRD. After 6 months, there is no evidence of disease recurrence, but longer follow-up is needed to demonstrate efficacy, and hopefully cure for this patient.

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