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Case Report

Relapsed Mantle Cell Lymphoma: Case Report and Review of Literature

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Abbreviations

MCL: Mantle Cell Lymphoma; RRVD: Rituximab, Revlimid, Velcade and Dexamethasone; VBR: Velcade, Bendamustine and Rituximab; CHOP: Cyclophosphamide, Hydroxydaunorubicin, Vincristine and Prednisone

The classical form of Mantle cell lymphoma (MCL) is classified as a mature B cell lymphoma. It is relatively uncommon comprising of 7-8 % of all Non- Hodgkins Lymphoma (NHL). The median age at presentation is 68 years and the vast majority present with advanced cases [1]. The hall mark of MCL is presence of translocation (11; 14) (q13; q32) leading de-regulated expression of Cyclin D1.

The initial therapy is dictated by the age and fitness of the patient. It is usually rituximab based chemo-immunotherapy followed by auto HSCT if clinically suitable. The median survival has recently improved from 3 years to 5-7years [2,3].

Case Presentation

A 63 years old was diagnosed of pulmonary tuberculosis from lung biopsy on 12 /11/2008. He was started on anti-tuberculosis (ATT) medications finished 1 year of ATT therapy. On follow up in pulmonary clinic in November of 2010 he was noted to have left sub mandibular Lymphadenopathy. He was referred to ENT. He initially had FNAC that showed atypical cells. He then had an excisional biopsy on 2/1/2011. Biopsy results came back as MCL. Patient was referred to hematology/oncology service in February 2011. He had staging work up with CT scan, bone marrow biopsy and cardiac function evaluation. He was staged as IIIA with MIPI score of 7.4 (high risk disease). He was deemed not fit for hyper CVAD protocol and was treated with CHOPR x 6 cycles with Intra-thecal prophylaxis. He tolerated therapy poorly with recurrent admissions for neutropenic fever. He finished 6 cycles of chemotherapy in June 2011. CT scan after 4 cycles showed Partial response (PR). Patient was noted to have new axillary and cervical lymphadenopathy in October 2011. Biopsy of right axillary lymph node was consistent with MCL. He was started on salvage chemotherapy with Velcade / Bendamustine and Rituximab (VBR) [1]on 27/10/2011. 2nd cycle was given on 6/12/11, cycle 3 on 11/1/12. Subsequently course was complicated by hemoptysis with right middle lobe consolidation. Patient was started on ATT empirically in 8/2/2011. Restaging was performed and noted to have a mixed response but significant progression of LNs in the mediastinum.He was switched to 3rd line therapy with Rituximab, Lenalidomide, Velcade and Dexamethasone (RRVD). He started cycle 1 on 25/3/12 after clearance from Infectious disease. CT scan after 2 cycles showed PR. Patient had interruption of therapy for febrile neutropenia. He was continued on cycle 5 in august 2012. In 8/12 had localized progression in right cervical LN. He was referred for external beam Radiotherapy.He received 36 GY in 18 Fractions starting 21/9/2012 and finished on 4/10/12. He restarted RRVD and finished 10 cycles on 18/12/2012. He was then started on maintenance therapy with Lenalidomide/Rituximab. He did well till September 2013 when he had progression of disease. He subsequently received another course of external beam radiotherapy for the symptomatic mediastinal lymph nodes (dysphagia). He was then referred to palliative care and expired in August 2014.

Discussion

There is no standard of care for patients with relapsed/refractory MCL. Salvage therapies using aggressive regimens like R-ICE, RDHAP or R-ESHAP may be suitable for patients with good performance status. There is consistent data about the effectiveness of Cytarabine in MCL so regimens like DHAP may be more useful.

Patients who are older or not physically fit are treated with relatively gentle therapies. Improvement in survival is due to activity of 2nd, 3rd and 4th line therapy [4] using novel agents. Therapeutic options include purine analogues [5-7] (Fludarabine, Cladribine) either as single agent or in combination, IMids (Thalidomide, Lenalidomide) [8] or Temsirolimus (mTOR inhibitor) [9] or Bendamustine [10]. Both Bortezomib (Velcade) [11,12] and Ibrutinib (BTK inhibitor) are FDA approved for relapsed MCL.

Although our patient was relatively young, he had poor performance status. He also had high risk disease with rapid progression after finishing induction therapy. Initial salvage was tried with VBR [12] though the response was suboptimal. At that point therapeutic options were limited to utilizing purine analogues (Fludarabine, Cladribine) either as single agent or in combination, IMids (Thalidomide, Lenalidomide) or Temsirolimus. Patient has no access to clinical trials especially those involving Ibrutinib (BTK inhibitor). As both Velcade and Revlimid are active in relapsed setting we postulated that combination should be active in this setting. RVd is an established regimen for Multiple myeloma with known toxicity profile. Prophylaxis with Acyclovir and Sulfamethoxazole/ Trimethorpim were given as recommended and continued in our patient. Our patient was successfully able to tolerate 10 cycles of RRVD and was placed on maintenance with Lenalidomide and Rituximab to control the disease. He was able to have a progression free interval of 10 months.

Our experience is limited to a single patient however the response

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was encouraging with easily tolerable side effects. Bortezomib was given subcutaneously. Neuropathy was limited to grade 1. No opportunistic infections were encountered throughout the course of the treatment. We hope that this regimen can be evaluated in a larger cohort to better assess the utility of this combination.

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