Salvage Chemotherapy with Mini-CVD + Inotuzumab Ozogamicin in a Patient with Relapsed Extramedullary BCR-ABL Negative B-cell Acute Lymphoblastic Leukemia

Presenting Author: Tony Joseph Kurian, MD, Hematology & Oncology Fellow, Hematology and Medical Oncology, USF Health, Moffitt Cancer Center, Tampa, FL

Co-authors: William Paul Skelton IV, MD, Hematology & Oncology Fellow, USF Health, Moffitt Cancer Center, Tampa, FL; Michael Jaglal, MD, Associate Program Director, Hematology & Oncology Fellowship, Moffitt Cancer Center, Tampa, FL

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Abstract

Introduction: Isolated extramedullary ALL relapse is rare and represents a challenging clinical scenario as patients with extramedullary disease are often excluded from clinical trials and there is limited data regarding optimal treatment strategies. Inotuzumab ozogamicin is a targeted therapy approved for relapsed ALL, and two case reports suggest extramedullary disease may respond to inotuzumab alone. A recent phase 2 clinical trial evaluated mini-hyperCVD + inotuzumab ozogamicin among patients with relapsed / refractory ALL. Mini-hyperCVD includes cyclophosphamide and dexamethasone at 50% dose reduction, no anthracycline, methotrexate at 75% dose reduction, and cytarabine at 0.5 g/m2 × 4 doses. We present the first known case of a patient with relapsed isolated extramedullary BCR-ABL negative B-cell acute lymphoblastic leukemia (ALL) treated with mini-hyperCVD + inotuzumab ozogamicin.

Case Presentation: The patient is a 58 year old male with a history of hypertension and atrial fibrillation initially diagnosed with B-cell acute lymphoblastic leukemia 3/2018 treated with 8 cycles of induction chemotherapy with hyper-CVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone, methotrexate, and cytarabine) along with 2 doses of intrathecal chemotherapy with each cycle which he completed 7 months after his initial diagnosis. The patient was unfortunately lost to follow up for 15 months before re-establishing care. Three months thereafter, he presented to the Emergency Department with right leg pain after a mechanical fall and was found to have a right leg hematoma on CT imaging. Further evaluation with MRI showed an infiltrative soft tissue mass within the right semitendinosus and semimembranosus muscles, compatible with an intramuscular neoplasm. He underwent biopsy of the mass which showed recurrent B-lymphoblastic lymphoma/leukemia (CD19+, TdT+, CD79a+, and CD10+). Repeat bone marrow biopsy was negative for malignancy, showing slightly hypocellular marrow (30%) with trilineage hematopoiesis and no significant increase in B-lymphoblasts. Staging imaging confirmed isolated extramedullary relapse of his ALL in his right lower extremity. He received 1 cycle of mini-hyper CVD + inotuzumab ozogamicin with plans to complete 3 cycles followed by restaging scans.

Discussion and Conclusion: Isolated extramedullary ALL relapse represents a challenging clinical scenario with little data available to guide management. The combination of systemic chemotherapy to inotuzumab may represent a strategy to limit the intozumab related side effects by decreasing the dose given while maintaining the potential effectiveness of inotuzumab against extramedullary disease and adding the potential benefits of systemic chemotherapy. This report represents the first known case of a patient with relapsed isolated extramedullary BCR-ABL negative B-cell acute lymphoblastic leukemia (ALL) treated with mini-hyperCVD + inotuzumab ozogamicin.

Learning Objectives
1. Discuss evidence-based approach for management of relapsed/refractory B-ALL
2. Examine novel treatment approach for management of isolated extramedullary relapse of B-ALL