A PEDIATRIC CASE OF TREATMENT-RELATED MYELODYSPLASTIC SYNDROME WHILE ON THERAPY FOR PRE-B ALL

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Research Abstract Title

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Describe role of Submitting/Presenting Trainee in this project (limit 150 words):

This is a Case Report describing a patient who I took care of while on my Bone Marrow Transplant Rotation. This patient was identified as one who was unique and would be a valuable case for learning for myself, as well as teaching others. I (the trainee), obtained consent from the patient and family to do a Case report, I read through this patient's clinical course and assembled the case report, with assistance from my mentors.

Background, Objectives/Goal, Methods/Design, Results, Conclusions limited to 500 words

Background: Treatment-related myelodysplastic syndrome (t-MDS) is a known, but rare, late effect of cancer therapy, specifically radiation, alkylating agents or topoisomerase II inhibitors. When secondary to treatment with alkylating agents, t-MDS typically occurs 4 to 7 years after therapy, and common cytogenetics include chromosomes 5 and 7 abnormalities. Treatment in children with t-MDS is typically allogeneic stem cell transplant, but the prognosis remains poor.

Objectives/Goal: To describe a rare case of a pediatric patient who developed t-MDS while receiving treatment for Pre-B Cell Acute Lymphoblastic Leukemia (pre-B ALL) and to outline the treatment regimen that he received.

Methods/Design: Case Report

Results: The patient is a 17-year-old male who was diagnosed with high risk pre-B ALL (CNS2) in November 2017. He received a standard 4-drug induction with negative MRD by flow cytometry at the end of induction. He continued the standard high-risk arm of AALL1131 and received 3000 mg/m2 cyclophosphamide.

While in cycle 6 of maintenance therapy, a routine CBC had 2.8% blasts. A bone marrow aspirate demonstrated severe erythroid and megakaryopoietic dyspoiesis with 13% myeloblasts by flow cytometry. There was no abnormal immature B-cell population. Chromosome analysis showed a reciprocal t(3;3)(q21.3;q26.2); GATA2, MECOM translocation with monosomy 7, consistent with diagnosis of t-MDS.

He completed 4 cycles of azacitidine prior to transplant and his blast percentage in the marrow decreased to 2%. His peripheral blast count cleared after completion of all 4 cycles of azacitidine. He received fludarabine, busulfan, melphalan and rabbit ATG as myeloablative conditioning for haplo-identical allogeneic bone marrow transplant. He received a CD34-selected, T-cell depleted transplant. On day +30 his marrow was negative for disease by flow cytometry and cytogenetics. On day +60 he started post-transplant decitabine maintenance therapy to prevent relapse. He completed 6 cycles of decitabine. Follow-up marrow evaluations after 2, 4 and 6 cycles have demonstrated no evidence of myelodysplasia or leukemia.

Conclusions: Alkylating agents, such as cyclophosphamide, are a known cause of t-MDS which can progress to AML. Generally, this occurs years after completion of therapy, however, this case demonstrates a rare instance of t-MDS developing on-therapy. There is room for improvement in treatment of t-MDS. Hypomethylating agents should be considered for use in patients with t-MDS prior to transplant, to limit additional chemotherapy in already heavily-treated patients. Maintenance therapy with hypomethylating agents post-transplant should be considered in patients at high risk of relapse.