BONE MARROW TRANSPLANT FOR MACROPHAGE ACTIVATION SYNDROME IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Background

The recognition of macrophage-activation-syndrome (MAS) in the setting of systemic-juvenile-idiopathic-arthritis (sJIA) is complex, but a necessary distinction given emerging treatment options. With overlapping clinical manifestations including fever, end-organ involvement and lymphadenopathy, there is a focus on laboratory values to differentiate MAS from a sJIA flare. Once parameters are met, multiple treatment modalities can be considered, as monotherapy or in combination, including steroids, immunosuppression, chemotherapy, intravenous immunoglobulin, and cytokine-directed biologics. Given the long-term morbidity and mortality associated with progressive inflammation and immune dysregulation due to MAS with sJIA, it is imperative to regain control over this complication. However, these treatments are not without their own adverse effects, and in this case presentation, those side effects overcame the benefits and led to bone-marrow-transplant (BMT).

Objectives

1. To describe the success of BMT in the setting of severely refractory MAS in sJIA.
2. To describe a possible genetic predisposition to severe disease: PLCG2 gene and HLA haplotyping.

Design/Method

Case report

Results

Our patient was initially diagnosed in 2018 with sJIA and quickly developed MAS, complicated further with interstitial lung disease (ILD). Experienced multiple mono- and combined therapy failures, escalating from NSAIDs, IL-1 blockade (anakinra and canakinumab), glucocorticoids, cyclosporine, IL-6 blockade, JAK inhibition, etoposide, and to emapalumab. Due to significant toxicity, most of the steroid-sparing medicines were stopped, except for anakinra and high dose steroids which were utilized for disease stabilization during the BMT process. A matched unrelated allogenic bone marrow transplant was completed in 10/2020. No evidence of graft-versus-host-disease and early ANC engraftment with stable mixed chimerism. At 2 years post BMT, patient has resolution of osteopenia, normalization of pulmonary function tests and normal inflammatory markers off medications. Genetic testing returned with a variable of unknown significance (VUS) in the PLCG2 gene that may contribute to refractory disease via PLAID/APLAID/FCAS3, an immune dysfunction syndrome spectrum including immune deficiency and autoinflammation. Also discovered an HLA haplotype associated with a hypersensitivity reaction to medications that can mimic inflammatory features of sJIA with higher relative risk for severe disease and/or lung complications, as seen with this patient.

Conclusion

In refractory cases of severe MAS in the setting of sJIA, with the possibility of genetic predispositions leading to further medication non-response and toxicity, a bone marrow transplant may be the best option for disease resolution.