Abstract Submission

19. Non-Hodgkin lymphoma Biology & Translational Research

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AN INCREASED RISK OF POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDER IN CHILDREN AFTER CARDIAC TRANSPLANTATION FOR CONGENITAL HEART DISEASE

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Background: Patients subjected to lifelong immunosuppressant therapy for solid organ transplantation are at an increased risk of developing malignancies. Post-transplant lymphoproliferative disorder (PTLD) represents the most common cause of malignancy seen in children after cardiac transplantation. The significance of pre-transplant cardiac diagnosis as a risk factor for PTLD in this population has not been previously investigated in depth.

Aims: This study aimed to examine the risk factors for development of PTLD specific to children undergoing cardiac transplantation.

Methods: We retrospectively reviewed the demographics, clinical features and outcomes of all 203 children (< 18 years), who received a heart transplant in our institution between January 2000 and December 2015. Kaplan-Meier method and Cox proportional hazards were used to assess the impact of prognostic factors including pre-transplant cardiac diagnosis on survival and freedom from PTLD.

Results: The study cohort consisted of 75 patients transplanted for congenital heart disease (CHD) and 128 patients for idiopathic cardiomyopathy (IC). The median follow up was 5.5 years. There was a significant difference in age at first invasive cardiac procedure via median sternotomy between children with CHD and IC (4 months vs 5 years, $p < 0.001$) but no difference in the age at transplantation between both groups ($p = 0.78$). PTLD was diagnosed in 15 (7.4%) children transplanted for underlying CHD (10/15) and IC (5/15) with a median age at diagnosis of 10.4 years (range; 6.6-14.0) and 11.5 years (range; 4.8-13.5) respectively. The median time to PTLD was 24 months (range; 10 - 50 months) with no significant difference in time to PTLD between patients with CHD and IC ($p = 0.09$). All tumour samples were Epstein Barr Virus (EBV) positive and of B-cell lineage. The histological subtypes consisted of 10 (67%) monomorphic lesions, 3 (20%) polymorphic, and 2 (13%) classical Hodgkin lymphoma. Early stage disease (stage I-II) was observed in 5 (33%) patients while advanced tumour (stage III-IV) was seen in the remaining 10 (67%) children. Overall freedom from PTLD was 96% at 1-year, 92% at 5-years and 90% at 10-years. The risk of PTLD was not significantly associated with age at transplantation, gender, ethnicity or type and number of immunosuppressants used ($p > 0.05$). Recipient EBV seronegativity prior to transplantation increased the risk of PTLD ($p = 0.04$) on multivariate Cox regression, while children with CHD had a significantly higher risk of developing PTLD compared to those with IC (Hazard Ratio= 5.3; 95% Confidence Interval= 1.5–18.9).

Summary/Conclusion: The identification of congenital heart disease as an important risk factor in the development of PTLD after paediatric heart transplantation is a novel finding. We posit that the underlying diagnosis of CHD is a potential proxy marker for early dysregulation of T cell mediated immunity occuring as a consequence of earlier thymectomies during invasive cardiac procedures in these patients compared to children with IC, predisposing them to primary EBV infection and aberrant proliferation of lymphoid cells. This hypothesis is supported by our study finding of a significant age disparity at the time of first invasive cardiac procedure via median sternotomy between children with CHD and IC, which warrants further investigation.

Keywords: Organ transplant, Post-transplant lymphoproliferative disorder, Risk factor