Cardiac Surgery as a Predictor of Cell mediated Immunity in Patients with 22q11.2 deletion syndrome

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BACKGROUND

22q11.2 deletion syndrome or DiGeorge syndrome (DGS) is known to have diminished thymic function or athymia with close 75% of cases having concomitant cardiac anomaly. Given the reduction of thymic tissue, it is expected that patients will have reduced T-cell function and have a stunted cell mediated immunity. Cardiac anomalies in DGS are surgically corrected within the first year of life and generally require the removal of thymic tissue to better access the underlying cardiac structures. As a result, these patients are often referred for immunologic screen tests to monitor T-cell activity in anticipation of development of a primary T-cell deficiency. Interestingly, studies have shown that only 2% of DGS patients have severe primary immunodeficiency. A portion of these patients had full athymia (previously known as complete DiGeorge syndrome) and studies indicated a benefit for these patients to receive thymus transplants on these patients. The remainder of the population does show decreased T cell subsets, specifically in the first two years of life.

OBJECTIVE

This was a retrospective study conducted to evaluate T cell function in patients with in the first two years of life with 22q11.2 deletion syndrome and assess the role of cardiothoracic surgery as stressor for stunting cell mediated immunity. This was done by measuring the difference between CD3, CD4, CD8, CD19, NK cells, CD45RA, CD45RO levels (ARUP T-cell subset panel 6) in the first 2 years of life in patients who were diagnosed with 22q11.2 deletion syndrome and comparing them to 22q11.2 deletion syndrome patients who did not undergo a cardiothoracic surgery.

METHODS

The study was comprised of a total of 46 patients diagnosed with 22q11.2 deletion syndrome via FISH. 24 of these patients underwent a cardiothoracic surgery and 22 patients who did not undergo any surgical procedure. Of the 24 patients who underwent cardiothoracic surgery, 9 patients had pre and post-surgery data to directly compare changes in T cell lines.

	mean difference (95% C.I) between first and last time point	p value (paired ttest, compar	outcome
No surgery	-1.273(-7.91-5.365)	0.678	CD3
	3(0.364-5.636)	0.03	CD4
	-3.273(-10.281-3.735)	0.323	CD8
	2.556(-4.374-9.485)	0.42	NK
	-1.8(-8.355-4.755)	0.55	CD19
Surgery			
	-6.1(-25.952-13.752)	0.505	CD3
	1.7(-9.372-12.772)	0.736	CD4
	-4.65(-12.428-3.128)	0.209	CD8
	0.4(-7.431-8.231)	0.911	NK
	-3.2(-13.788-7.388)	0.511	CD19
	* negative value means improvement		
	*positive value means decrease in lab test		

Among patients without surgery, there is significant decrease in CD4 percent from the baseline. We found no significance changes between the first and at time points and second time points. Among patients with surgery, we found no significance changes between the first and last timepoints

RESULTS

Our results showed that there was no significant difference in any of the T cell lines, with the Exception of CD4 in the control group. When comparing the pre and post T cell levels, there was no significant change in the lab values. For those patients who had T cell levels that where below normal range, only 1 patient presented with frequent infections and was immunocompromised (perhaps had true thymic aplasia with little extrathymic T cell differentiation). Among the patients who did not undergo cardiothoracic surgery, there was a significant decrease in CD4% from the baseline (P=0.03). This is likely due to a small population size. Removal of thymic tissue did not play a significant role in alteration of the cell mediated immunity. When examining the T cell levels past the age of two in the patients of this study, only one patient was truly immunocompromised with no increase in T cell levels. This can be correlated to the general population of 22q11.2 deletion where 2% of the population truly have a stunted cell mediated immunity.

CONCLUSIONS

It is likely that the majority of DGS patients do not present with severe primary cell mediated immunodeficiencies because their altered immune system compensates with extrathymic T cell differentiation. Maintenance of cell-mediated immunity has been documented in DGS patients that have undergone cardiac surgery in previous studies but never prior to the age of two. A study that assessed the long-term pattern of T cell populations in DGS indicated that a deterioration of T-cell number or function did not occur overtime. The results and conclusions of this study warrant further investigation with a larger population size. It would also be beneficial to investigate T cell levels in patients who underwent similar studies but where not diagnosed with 22q11.2 (who likely have less extrathymic T cell differentiation). However, from this novel retrospective study, we can conclude that frequent testing of T cell levels in the first two years of life, for the reason of cardiac surgery being a stressor on cell mediated immunity, is not indicated.

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