

PREVALENCE OF GENETIC TESTING IN SCIMITAR SYNDROME

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Background: Scimitar syndrome (SS) is a rare congenital heart defect composed of partial anomalous pulmonary venous connection from the right lung, via a scimitar vein, to the inferior vena cava rather than the left atrium. SS is often associated with right lung hypoplasia and related pulmonary pathology. The prevalence of SS is roughly 1 in 50,000 live births. Genetic associations in SS have not been well-investigated at present.

Materials/Methods: We included all patients with SS at our institution from January 1987 to July 2019. All charts were evaluated to determine if genetic testing was performed, including chromosomal microarray (CMA) or gene sequencing including whole-exome sequencing (WES). For CMA and WES results, changes identified as pathogenic/likely pathogenic and variants of unknown significance were collected.

Results: In total, we identified 77 patients with SS (68% female). CMA was performed in 17 patients, demonstrating two pathogenic variants, including a duplication in the 22q11.21 region involving proximal DiGeorge critical region but not TBX1 in one patient, and a duplication in 10q21.3q23.1 consistent with 10q22-q23 deletion syndrome in the other. Five variants of unknown significance were also noted on CMA testing. WES was performed in five patients, revealing three patients with pathogenic variants. One patient was identified to have a de novo EP300 variant causing Rubinstein-Taybi type 2, one patient had a de novo MYRF variant (which has a newly-reported association with SS), and one patient had a NAA15 pathogenic variant (known association of cardiac anomalies and heterotaxy syndrome). Thus, a total of five of 17 tested patients (29%), comprising 6% of the cohort, were found to have pathogenic variants.

Conclusions: In a cohort of patients with SS from our center, 22% of patients underwent genetic testing, and almost a third of these were noted to be pathogenic findings. Alterations in transcription factors, glutamate receptor subunit and histone binding were seen in our cohort. Given the relatively high prevalence of genetic variants and little knowledge of the pathophysiology, we recommend further genetic investigation in patients with SS. This will aid in counseling for other co-morbid findings and regarding future pregnancies, and will allow for more detailed outcome studies stratified by specific genetic conditions.