Importance of Genetic Evaluation in Pediatric Restrictive Cardiomyopathy

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Introduction

- Restrictive cardiomyopathy (RCM) is characterized by:
  - Severely impaired ventricular relaxation
  - Normal or near normal systolic function
  - Normal or near normal wall thickness

- Etiologies of pediatric RCM are poorly understood
  - Majority of cases are idiopathic[1,2]
  - ~30% reported with prior family history[3]

- Sarcomeric and cytoskeletal mutations have been implicated in prior small studies

- **We sought to review the yield of commercially available genetic testing in children with RCM at our center**

Methods

- Single-center retrospective review
- Children <18 years old diagnosed with RCM between 1988 and 2012
- Data collected: basic demographics, family history, echocardiographic data, explant pathology and results of commercially available genetic testing panels
- Descriptive statistics

Disclosures

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Results

Demographics	n (%)
Total pts with RCM	20
Male	12 (60%)
Median age at dx, Yrs (Range)	5.9 (0.5-16.2)
Presenting Symptoms	
Cough	8 (40%)
Dyspnea	6 (30%)
Tachypnea	6 (30%)
FTT	4 (25%)
Syncope	3 (15%)
Phenotype	
RCM	14 (70%)
RCM/DCM	5 (25%)
RCM/HCM	1 (5%)

Genetic Evaluation	n (%)
Genetic testing performed	
Yes	12 (60%)
*No**	8 (40%)
Positive genetic testing	6/12 (50%)
TNNI3	4
MYH7	1
DES	1
Positive family history of CM	
+ testing	2/6
- testing	0/6
No testing	0/8
Additional genetic variants identified	
Multiple variants of unknown significance (TTN, TPMO, TNNI3)	1
Benign polymorphism of ZASP	1
Seckel syndrome (RCM not previously described with Seckel syndrome)	1

* 7 patients cared for prior to availability of commercially available testing
1 patient's testing denied by third party payer

- Explant pathology suggestive of a mitochondrial disorder in 2 cases (both with negative genetic testing)

Discussion

- Common symptoms at diagnosis of RCM are pulmonary— related to pulmonary venous congestion
- Genetic testing identified positive mutation in 50% of patients tested but also identified 1 pt with variants of unknown significance
  - Implications for family screening/follow-up
- Limitations:
  - Era effect in genetic testing with 7/8 patients not tested due to lack of available testing

Conclusions

- ***RCM can be an expression of sarcomeric and cytoskeletal mutations in children***
- ***Genetic evaluation using currently available sarcomeric and cytoskeletal panels may define a genetic etiology in up to 50% of pediatric patients tested***
- ***These results support recent guidelines[4] encouraging the use of genetic testing to help identify heritable forms of cardiomyopathy***

References

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