Surveillance of Cardiac Arrhythmias in Paediatric Patients with Myotonic Dystrophy Type 1

Tsang AC 1, Lazarev Y 1, Lougheed J 2, McMillan HJ 1,2
1. University of Ottawa Faculty of Medicine; 2. Children’s Hospital of Eastern Ontario

Objectives
- To determine the prevalence of cardiac arrhythmias within the population of DM1 patients that received care at Children’s Hospital of Eastern Ontario during a 24 year time period (1990-2014).
- The occurrence and type of cardiac arrhythmia will be identified and severity of diagnosis, indicated by the number of cytosine-thymine-guanine (CTG) triplet repeats in the patient and first degree relatives that have undergone genetic testing.

Background Information
- Myotonic dystrophy type 1 is a autosomal dominant neuromuscular disorder caused by a trinucleotide CTG repeat expansion mutation in 19q13 involving skeletal muscle, respiratory and cardiac systems.1
- The development of cardiac arrhythmia in the younger subset of these patients is thought to be uncommon and their relationship to the manifestation of other disease findings is unclear.1,4,5
- Patients with DM1 are at an increased risk of sudden cardiac death primarily from atrioventricular block.3
- Sinus bradycardia, tachyarhythmias such as atrial flutter, ventricular tachycardia and atrio fibrillation, and atrioventricular and intraventricular conduction blocks have been reported in paediatric patients and in neonates with DM1.1,4,5,6,7

Methods: Retrospective Cohort Study
- Population: Paediatric patients diagnosed with DM1 between (January 1990 – May 2014) at the Children’s Hospital of Eastern Ontario will be eligible for entry into the study.

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Age 0-18 years at time of diagnosis</td>
<td>1) Incomplete medical records and/or unavailable genetic diagnosis</td>
</tr>
<tr>
<td>2) Myotonic dystrophy diagnosed via genetic testing indicating ≥50 CTG repeats at CHEO Jan 1990 – May 2014</td>
<td>2) Cardiac disease not associated with a diagnosis of myotonic dystrophy type 1</td>
</tr>
<tr>
<td>3) Patient must have undergone ECG, Holter monitor, echocardiogram or exercise stress test</td>
<td>3) Presence of contractures</td>
</tr>
</tbody>
</table>

- Primary Indicators of disease: Evidence of cardiac arrhythmia documented at least once on electrocardiogram (ECG) or Holter monitor (24H ECG).
- Secondary Indicators of disease : Evidence of anatomical abnormalities in the heart seen on echocardiogram.

Results

Characteristics of patients with Myotonic Dystrophy (Type 1) in the CHEO cohort
- Between 1990-2014, 38 patients were followed at CHEO for DM1
- Genetic testing confirmed CTG repeat expansion in 35/38 (92%)
- Median age at diagnosis was 30.5 months old
- 26 of the patients had a mother that was diagnosed with DM1
- 2 of the patients had a father diagnosed with DM1 (4 unknown)
- 10 patients had siblings that had been diagnosed with DM1

Cardiac Abnormalities
- 12 patients were found to have abnormal results on electrocardiogram (ECG)
- 14 patients were found to have an abnormal cardiac ECHO
- No patients were started on prophylactic medications during the retrospective review period

Abnormalities found on ECHO cardiogram
- Atrial Septal Defect ( Patent Foramen Ovale) 9
- Patent Ductus Arteriosus 4
- Tricuspid Regurgitation (mild) 2
- Ventricular Septal defect 1
- Asymmetric thickening of intraventricular septum 1
- Myomatous Mitral Valve (asymptomatic) 1

Respiratory Disease
- 13 patients were found to have respiratory disease:
- 10 patients were reported to have an abnormal sleep study

Abnormalities found through serial ECG testing
- Left Ventricular Hypertrrophy +/- L-axis deviation 5
- Right Ventricular Hypertrrophy +/- R-axis deviation 7
- 1st Degree AV block 2
- 2nd Degree Heart Block Type 1 (Wenkebach) 1
- Non specific Q wave changes 2
- Non specific T wave changes 2
- Non specific intraventricular conduction delay (LBBB) 5
- Wolff-Parkinson White 1
- Supraventricular Tachycardia 1

Abnormalities found through serial ECG testing
- Obstructive sleep apnea 6
- Central Sleep Apnea 4
- Apneic spells 5
- Obstructive Airway Disease and asthma 3
- Nocturnal hyperventilation 3
- Other (bronchopulmonary dysplasia) 1

Developmental Milestones
- 34 of 38 patients were found to have a developmental delay and subsequent intellectual disability or learning impairment

<table>
<thead>
<tr>
<th>Median Age to meeting Developmental Milestones (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sitting Independently (n=17)</td>
</tr>
<tr>
<td>Walking Independently (n=26)</td>
</tr>
<tr>
<td>First Words (n=18)</td>
</tr>
<tr>
<td>Construction of 2 word phrase (n=18)</td>
</tr>
</tbody>
</table>

Discussion and Conclusion
- Children with myotonic dystrophy have significant global developmental delay.
- Two cases of paternally-inherited of DM1 were found.
- DM1 is typically inherited from the maternal allele.
- Two significant cardiac arrhythmias were identified in 2 of 38 patients in our study (Wolff-Parkinson-White and second degree heart block).
- The occurrence of cardiac arrhythmias is less common in children and adolescents with DM1. Only 5% of our population had significant cardiac arrhythmias.
- Adult patients with myotonic dystrophy are much more likely to demonstrate cardiac arrhythmia (20-40%). 30% of mortality in adults with DM1 are due to a cardiac cause.11
- Current surveillance for cardiac arrhythmia in this population closely follows the standard of practice in adult patients, but no such standard has been established in paediatric care.

Key Findings on Myotonic Dystrophy Type 1 in Paediatric Patients
- Clinicians should be aware of an increased prevalence of conduction abnormalities in children with DM1. Cardiac complaints should illicit increased awareness. (Level C)
- Children with DM1 are more likely to have intellectual disability. Increased support for education and development should be initiated (level C)

References