Cardiac involvement in myotonic dystrophy

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Background: Myotonic dystrophy (DM) is an inherited progressive muscle disorder caused by defects in muscle proteins. As the incidence of this condition is low, not many are familiar with the multisystem involvement. At times, cardiac disease may even be the predominant manifestation in the form of arrhythmias, conduction defects, and cardiomyopathies. The progression of the disease can lead to sudden, unpredictable death. Thus, it is important to identify this subgroup and treat accordingly.

Objective: To identify patients with DM and assess their risk for sudden cardiac death.

Methods: Nine patients previously diagnosed with muscular dystrophy were evaluated by cardiologists for various reasons, from a general follow-up to cardiac arrest. All of them had electrocardiograms (EKG) and 2-D echocardiograms, and seven of them had further electrophysiological (EP) studies.

Results: Of the nine patients with DM, eight had EKG evidence of conduction abnormalities ranging from first-degree heart block to complete heart block. Of the seven who had EP studies, five had inducible ventricular tachycardia requiring immediate cardioversion and implantable cardioverter defibrillator (ICD) implant. Two of them underwent permanent pacemaker placement due to complete heart block and infra-Hissian block. The remaining two patients opted for a conservative approach with yearly EKG monitoring.

Conclusion: Because one-third of the cardiac deaths in patients with DM are sudden, there is a strong need to identify these patients and intervene in those at high risk. Prophylactic pacemaker placement is recommended even in those with minimal conduction system abnormality. However, the common practice is to identify patients at high risk of conduction abnormalities by EP studies and then provide them with prophylactic invasive strategies.

Keywords: myotonic dystrophy; electrophysiology study; heart block; arrhythmia; sudden death

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In this case series, we present nine cases of DM in a small, community-based teaching hospital that presented with various cardiac manifestations and received appropriate interventions, to prevent death from sudden cardiac arrest.

Case reports

Case 1
An 82-year-old Caucasian woman with a medical history of hypertension and DM presented with episodes of recurrent lightheadedness, dizziness, and near syncope. The 12-lead EKG showed a rate of 69 beats per minute (bpm), first-degree AV block with a PR interval of 244 milliseconds (ms), and a left axis deviation. There was an intraventricular conduction defect (IVCD) with a left bundle branch (LBBB) like morphology and QRS duration of 163 ms. The corrected QT interval was 432 ms. A 2-D echocardiogram showed a non-dilated left ventricle with mild, concentric hypertrophy (LVH) and paradoxical septal wall motion abnormalities with an estimated left ventricular ejection fraction (LVEF) of 60%. Pharmacologic single-photon emission computed tomography (SPECT) nuclear images with LEXI SCAN revealed no significant evidence for myocardial ischemia or transmural myocardial infarction.

In view of these findings and the absence of an alternative diagnosis for her dizziness, she was considered at high risk for progression of cardiac conduction system abnormalities, given her history of DM. She was referred for a diagnostic EP study, which revealed a normal sinus node function, but a severely prolonged HV interval (104 ms). There was no evidence of a dual AV node physiology or an accessory pathway, but VA conduction was present. Sustained, fast, polymorphic ventricular tachycardia was easily induced, signaling that in addition to being at high risk for complete heart block and asystole, she was at significant risk for sudden cardiac death due to sustained malignant ventricular tachycardia. She, therefore, underwent a dual chamber ICD system placement.

Case 2
A 57-year-old Caucasian woman with a history of hereditary hair loss and dystonia presented to the hospital with increased generalized weakness and progressive difficulty ambulating for the last 2 years. The patient was clinically diagnosed with DM which was confirmed with an EMG and nerve conduction studies. A 12-lead EKG revealed a sinus rhythm, first-degree AV block with PR interval of 309 ms, left axis deviation, and an IVCD of LBBB block-like morphology with a QRS duration of 170 ms. Echocardiogram demonstrated a non-dilated left ventricle with mild hypertrophy and paradoxical septal wall motion abnormalities and an estimated LVEF of 65%. A pharmacologic SPECT nuclear stress test showed no significant fixed or reversible perfusion defect suggestive of myocardial ischemia or myocardial infarction. Due to the patient’s diagnosis of DM and her presenting symptoms, a diagnostic EP study was performed. She had a severely prolonged HV interval (94 ms) as well as both sinus and AV nodal dysfunction. Furthermore, there was evidence for infra-Hissian block. There was no evidence of a dual AV node physiology or an accessory pathway and no VA conduction. Although a few runs of non-sustained ventricular tachycardia were seen during ventricular programmed stimulation, no sustained ventricular tachycardia could be induced, suggesting a need for a dual chamber permanent pacemaker for prevention of sinus arrest and complete heart block.

Case 3
A 42-year-old man with a history of DM presented with complaints of dyspnea and fatigue as well as palpitations. A 12-lead EKG showed a rhythm of sinus origin at a rate of 100 bpm. The PR interval was 178 ms and QRS duration was 99 ms. There was a non-specific IVCD with an rSr’ pattern in lead V1. The 24-hour EKG monitoring showed sinus rhythm with an average heart rate of 88 bpm and occasional premature atrial and ventricular beats. An echocardiogram demonstrated a non-dilated left ventricle with mild concentric hypertrophy and an estimated LVEF of 50%. A pharmacologic stress test showed no significant evidence of myocardial ischemia or myocardial infarction and a well-preserved left ventricular systolic function with a calculated ejection fraction of 70%. An electrophysiology study showed prolonged HV interval (72 ms) with normal sinus and AV node function at baseline. There was no evidence of a dual AV node physiology or accessory pathway, but VA conduction was present. After administration of procainamide, his HV interval prolonged to 99 ms, suggesting severe conduction system abnormalities at the His bundle systems level. Sustained polymorphic ventricular tachycardia was easily induced during a ventricular programmed stimulation, requiring immediate cardioversion, and suggesting a need for a dual chamber ICD system for the prevention of sudden cardiac death due to complete heart block and/or malignant ventricular tachyarrhythmia.

Case 4
A 35-year-old woman with a family history of coronary artery disease, arrhythmia, and heart block presented with recurrent episodes of lightheadedness, dizziness, and near-syncope. She had a history of type I DM and an abnormal EKG. She, therefore, was referred for a cardiac EP study. A 12-lead EKG showed a rhythm of sinus origin, first-degree AV block with a PR interval of 238 ms, and QRS duration of 105 ms. There was no V A conduction. Although a few runs of non-sustained ventricular tachycardia were seen during ventricular programmed stimulation, no sustained ventricular tachycardia could be induced, suggesting a need for a dual chamber permanent pacemaker for prevention of sinus arrest and complete heart block.
Her left ventricular systolic function was well preserved with an estimated LVEF of 55–60%. A pharmacologic nuclear stress test revealed no evidence of myocardial ischemia or infarction. An EP study showed normal sinus node function coupled with a severely prolonged HV interval (101 ms). Although there was dual nodal physiology documented, no accessory pathway was identified. Sustained, monomorphic, ventricular tachycardia was easily induced during ventricular-programmed stimulations, suggesting potential benefit from a dual chamber ICD system for the prevention of sudden cardiac death due to a high-grade heart block and/or malignant sustained ventricular tachyarrhythmia.

**Case 5**

A 47-year-old man with a history of severe peripheral arterial disease, cerebrovascular disease, mild coronary artery disease, and DM was referred for a cardiac evaluation prior to vascular surgery for ischemic arterial leg ulcers. He also has multiple family members with DM and bradycardia requiring permanent pacemakers. His 12-lead EKG showed sinus rhythm with first-degree AV block and a PR interval of 208 ms. There is an IVCD with an rSr’ pattern in V1-V2 leads and a QRS duration of 90 ms. An echocardiogram showed a non-dilated left ventricle with well-preserved systolic function and an estimated left ventricle ejection fraction of 55–60%. Because the patient had a history of DM and an abnormal electrocardiogram, he was advised to have an EP evaluation. Currently, he has not completed his EP study.

**Case 6**

A 63-year-old woman with a history of hypertension, diabetes mellitus, and DM presented with shortness of breath, chest pain, and severe bradycardia. She had a brother with DM, who died suddenly at the age of 50. Her presenting 12-lead EKG revealed a rhythm of sinus origin with complete heart block and a ventricular escape rate of 40 bpm. There was an IVCD of LBBB-like morphology and QRS duration of 108 ms. An echocardiogram showed a non-dilated left ventricle with normal systolic function and an estimated LVEF of 55–60%. She declined an EP study and received a permanent pacemaker due to a symptomatic complete heart block and severe bradycardia.

**Case 7**

A 52-year-old woman with a history of DM presented with recurrent falls and dysphagia and worsening symptoms of DM. She also had multiple family members with DM and a sister requiring a defibrillator. EKG showed normal sinus rhythm with PR interval of 120 ms with no evidence for conduction abnormalities. Echocardiogram showed non-dilated left ventricle with ejection fraction of 55% and she elected for yearly monitoring with 12-lead EKG.

**Case 8**

A 57-year-old woman with history of coronary artery disease and DM presented with chest pain from an acute anterior wall myocardial infarction, which was complicated with cardiac arrest and asystole. She required temporary cardiac pacing and EKG showed sinus rhythm with PR interval of 180 ms, QRS duration of 146 ms, RBBB and LAFB along with 3 mm ST segment elevation in the anterior leads. An emergent coronary angiography was done which showed total occlusion of the LAD, which was subsequently stented. Given the cardiac arrest and history of DM, a diagnostic EP study was done which showed an abnormal sinus node and AV node function with prolonged HV interval of greater than 120 after procainamide infusion. In view of easily inducible sustained monomorphic ventricular tachycardias, cardioversion with an ICD system implantation was done.

**Discussion**

Cardiac involvement in any of the primary muscular disorders is common, although the exact percentage of involvement varies depending on the literature. It can present in many different forms such as echocardiographic abnormalities, rhythm disturbances, conduction abnormalities, myocardial abnormalities, secondary valve insufficiencies, or even thrombogenic states (9). In some circumstances, these cardiac abnormalities are potentially life threatening. Thus cardiac evaluation is an important aspect of the clinical management of these patients.

In particular, cardiac conduction defects of varying degrees of severity are common in patients with DM. In one series, 90% of individuals had conduction defects (2), which can be a significant cause for early mortality in...
| No | Sex | Age | Clinical presentation | Diagnosis | EKG | 2D echocardiogram | HV interval | SA node function | Arrhythmia | Device implant |
|----|-----|-----|-----------------------|-----------|-----|-------------------|-------------|-----------------|------------|----------------|
| 1  | F   | 82  | Lightheadedness, dizziness and near-syncope | Myotonic dystrophy | SR  | Non-dilated LVH | 104 | Normal | Normal | ICD |
|    |     |     |                       |           | PR 277 ms | EF 60% | | | | |
|    |     |     |                       |           | QRSd 164 ms | | | | | |
|    |     |     |                       |           | IVCD (LBBB) | | | | | |
| 2  | F   | 57  | Generalized weakness and progressive ambulatory dysfunction | Myotonic dystrophy | SR  | Non-dilated LVH | 94 | Abnormal | Infra-Hissian block | PPM |
|    |     |     |                       |           | PR 309 ms | EF 65% | | | | |
|    |     |     |                       |           | QRSd 170 ms | | | | | |
|    |     |     |                       |           | IVCD (LBBB) | | | | | |
| 3  | M   | 42  | Dyspnea and fatigue | Myotonic dystrophy | SR  | Non-dilated LVH | 72 | Abnormal | Infra-Hissian block | ICD |
|    |     |     |                       |           | PR 178 ms | EF 50% | | | | |
|    |     |     |                       |           | QRSd 99 ms | | | | | |
|    |     |     |                       |           | IVCD (rSr' V1-2) | | | | | |
| 4  | F   | 35  | Recurrent lightheadedness, dizziness and near-syncope | Myotonic dystrophy Type 1 | SR  | Non-dilated LVH | 101 | Normal | Normal | ICD |
|    |     |     |                       |           | PR 238 ms | EF 55% | | | | |
|    |     |     |                       |           | QRSd 105 ms | | | | | |
|    |     |     |                       |           | IVCD | | | | | |
| 5  | M   | 47  | Weakness and Fatigue | Myotonic dystrophy Type 1 | SR  | Non-dilated LV | – | – | – | – |
|    |     |     |                       |           | PR 208 | EF 60% | | | | |
|    |     |     |                       |           | QRSd 90 ms | | | | | |
|    |     |     |                       |           | IVCD (rSr’ in V1-V2) | | | | | |
| 6  | F   | 63  | Chest pain, Shortness of breath, Bradycardia | Myotonic dystrophy Type 1 | CHB | Non-dilated LV | >150 | Normal | CHB | PPM |
|    |     |     |                       |           | QRSd 108 | EF 60% | | | | |
|    |     |     |                       |           | IVCD (LBBB) | | | | | |
| 7  | F   | 53  | Recurrent lightheadedness, dizziness, near-syncpe/syncope | Myotonic dystrophy | SR  | Dilated LV | 47 | Normal | Abnormal | ICD |
|    |     |     |                       |           | PR 200 ms | LVH | | | | |
|    |     |     |                       |           | QRSd 140 ms | EF 35% | | | | |
|    |     |     |                       |           | IVCD (RBBB) LAHB | | | | | |
| 8  | F   | 57  | Chest Pain, cardiac arrest | Myotonic dystrophy 1 | SR  | Non-dilated LVH | 50% | Abnormal | Abnormal | ICD |
|    |     |     |                       |           | PR 180 ms QRSd 146 ms RBBB and LAFB | EF 65% | | | | |
|    |     |     |                       |           | 1st degree AV Block | | | | | |
| 9  | F   | 52  | Dysphagia, muscle weakness | Myotonic dystrophy 1 | SR  | Non-dilated LV | 60% | Normal | Normal | – |
|    |     |     |                       |           | PR 232 ms QRSd 100 ms | EF 60% | | | | |

IVCD, intraventricular conduction delay; VA, ventricular atrial; AV, atrioventricular; EKG, electrocardiogram; LVEF, left ventricular ejection fraction; SPECT, single-photon emission computed tomography; ICD, implantable cardioverter-defibrillator.
individuals with DM1, and sometimes can be associated with sudden death. It therefore becomes very important for early detection and appropriate treatment in these high risk individuals. Because progression of conduction system abnormalities is not always predictable, and there is a high possibility of ventricular arrhythmia, diagnostic EP studies are paramount in identifying such high risk individuals (4).

In this case series, we have presented nine patients with DM having an underlying cardiac manifestation. The clinical presentation ranged from mere weakness to full-blown features of DM. The diagnosis was made on clinical grounds and confirmed with genetic testing in most cases prior to our interaction. The most common initial EKG abnormalities in our patients were first-degree AV block and non-specific IVCDs. Generally, His-Purkinje conduction abnormality is the most frequent EP abnormality (10) but patients can also present with symptomatic conduction system abnormalities, which have been demonstrated in Table 1.

Severe conduction system abnormalities are defined as: any rhythm other than sinus, a PR interval more than 240 ms, a QRS duration over 120 ms, or a second- or third-degree AV block; and all are independent risk factors of sudden death (8). Therefore, a 12-lead EKG is an appropriate screening test and should be performed annually after the diagnosis of DM. In our patients, echocardiography studies showed evidence of left ventricular myocardial prominence, which may not necessarily be related to underlying hypertrophic cardiovascular diseases. Pharmacologic nuclear SPECT imaging can exclude significant evidence for structural or epicardial coronary artery diseases.

Despite the latest consensus guidelines for prophylactic device therapy in DM patients with minimal conduction abnormalities, prophylactic pacing is rarely done based on the first observation of a conduction defect (11). EP studies are instrumental in identifying high risk patients. A recent retrospective study showed that patients who underwent invasive strategies (cardiac pacing/ICD) had lower mortality with significantly higher survival rate in a 9-year follow up (12), however, no prospective, randomized, clinical study to date has demonstrated long term benefit (10). In our study, six patients had HV intervals greater than 72 ms and five had inaducible, sustained, ventricular tachycardia requiring immediate cardioversion and received an ICD. Five of them required a dual chamber ICD system despite an abnormal QRS duration (IVCD) and infra-Hissian block which usually requires permanent pacemaker only. We can attribute this to the sustained inducible ventricular arrhythmia which puts patients at high risk of sudden cardiac death. Two of them required permanent pacemaker placement due to complete heart block and infra-Hissian block. These EP findings are typical in patients with DM.

Conclusion
In patients with DM, approximately one-third of the cardiac-related deaths are due to sudden death and the bulk of these can be prevented by prophylactic cardiac devices. A majority of these high-risk patients can be identified if the physician is aware and monitors them with yearly EKGs, looking for any changes. Appropriate intervention with prophylactic invasive strategies may help avoid catastrophic outcomes. Identifying such patients may be difficult unless there is increased awareness among our primary care physicians, hospitalists, and neurologists who interact more often with these patients.

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The authors have no conflict of interest to report.

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