

Progressive conduction disturbance in myotonic dystrophy

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Abstract

Myotonic dystrophy (DM), the commonest dystrophy in adults, is an autosomal dominant disease characterized by a variety of multisystemic features. Two main genetically distinct forms of DM have been identified: type 1 (DM1), the classic form first described by Steinert, and type 2 (DM2), identified by Ricker. DM1 is caused by trinucleotide expansion of cytosine-thymine-guanine (CTG) in the myotonic dystrophy protein kinase gene, whereas in DM2 the expansion of tetranucleotide repeats (CCTG) in the zinc finger protein 9 gene was identified. Both mutations are dynamic and are located in non-coding parts of the genes. Phenotype variability of DM1 and DM2 is caused by a molecular mechanism due to mutated RNA toxicity. DM1 is characterized by myotonia and multi-organ damage with major cardiac involvement. The disease is usually slowly progressive and life expectancy is reduced by the increased mortality associated with cardiopulmonary complications. Sudden death can occur as a consequence of cardiac-conduction abnormalities. We present the ECG of a 26 year-old male with DM1 and progressive conduction system disturbance characterized by syncopal episodes. (Cardiol J 2011; 18, 3: 322–325)

Key words: myotonic dystrophy, syncope, atrioventricular block, sudden death

Electrocardiographic description

This is a 12-lead electrocardiogram (ECG) of a 26 year-old male patient with myotonic dystrophy type 1 (DM1) diagnosed eight years previously, with severe distal muscular weakness, gait, speech and mastication disorders, and mild mental retardation. A positive family history with similar manifestations was present (mother and brother, the latter presenting with sudden death at the age of 34). Two years ago, our patient had a cholecystectomy with prophylactic temporary pacemaker implantation during surgery, due to severe conduction system disturbances (Fig. 1A).

He was admitted to the intensive care unit due to a syncopal episode of one minute's duration. He had suffered diarrhea for the previous four days. On admittance, the patient was in no distress, with amnesia of the syncopal episode. Heart rate was 50 bpm, blood pressure was 110/70 mm Hg and he was afebrile. Remarkable features of his physical examination were myotonia of the tongue and extremities. Cardiovascular, respiratory and abdominal examination was unremarkable. Lab tests showed hypomagnesemia (1.1 mg/dL, range: 1.5–2 mg/dL) and hypocalcemia (7.1 mg/dL, range: 8.5–10.5 mg/dL). The baseline ECG showed sinus bradycardia (heart rate 40 bpm), left atrial enlargement, first-

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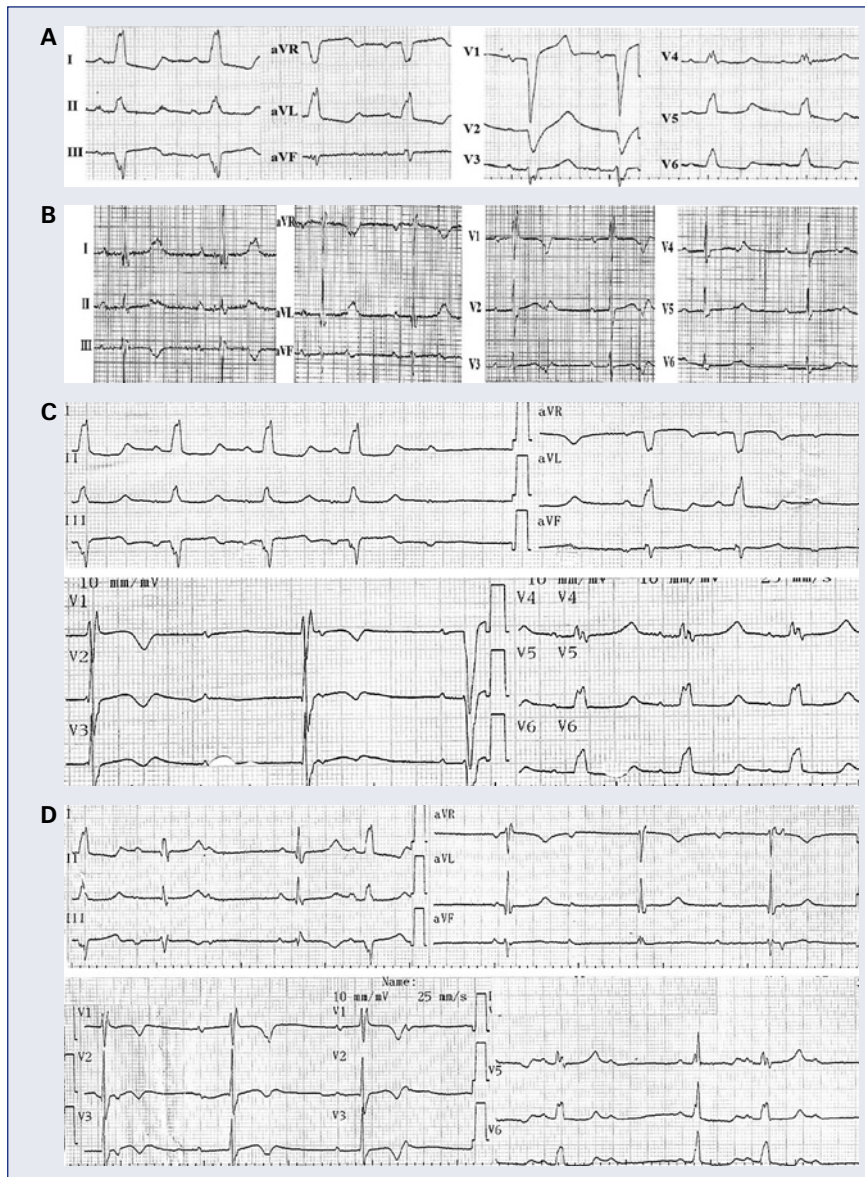


Figure 1: Electrocardiogram description. **A.** Classical left bundle branch block (LBBB) pattern, supraventricular command (sinus rhythm), normal PR interval (160 ms), QRS axis near 0° (frequent in LBBB), QRS duration of 160 ms. QRS complex of the rS type in right precordial leads, monophasic, broad notched or slurred R wave in the left leads (I, aVL, V5, V6), R-peak time or intrinsicoid deflection in I, V5–V6 ≥ 60 ms but normal in V1–V2 and V3, characteristic absence of initial q waves in leads I, V5 and V6. ST-T opposite to a greater deflection of QRS: positive from V1 to V4 and negative in left leads I, aVL, V5 and V6. These are alterations secondary to ventricular repolarization with wide QRS-ST-T angle and normal ventricular gradient; **B.** Incomplete right bundle branch block (IRBBB) and second degree AV block. Conducted P waves showing PR interval prolongation (from 240 to 280 ms) suggesting 2nd degree AV block Mobitz type II; **C.** Frontal plane leads I, II and III showing sinus rhythm with LBBB QRS morphology in the first three beats. The fourth P wave is not conducted (P wave not followed by a QRS complex), aVR, aVL and aVF shows only two normal P-QRS complexes with LBBB pattern. The fourth beat shows a P wave not followed by correspondent QRS complex. Precordial leads show complete AV dissociation; ventricular heart rhythm 34 bpm and atrial heart rhythm 62 bpm. QRS pattern: wide QRS complexes with left leads showing LBBB pattern and V1 triphasic QRS broad (150 ms) pattern suggestive of IRBBB (alternating bundle branch block); **D.** Complete AV block with QRS complexes showing alternating bundle branch block (LBBB and RBBB). From V4 to V6, we observe three QRS complexes with unequal degrees of LBBB, indicating no advanced or complete LBBB.

-degree atrioventricular (AV) block (PR interval of 280 ms), incomplete right bundle branch block, and prolonged QTc interval (QTc = 508 ms). During the admission, the electrolytic disturbance was corrected. During the following 24 hours, the patient experienced a fresh syncopal episode while at rest. The ECG showed heart rate of 35 bpm with complete AV block, alternating bundle branch block pattern (right and left bundle branch block; Figs. 1C, D). A permanent pacemaker was implanted.

Points to ponder

DM1, first described by Steinert, is the most frequently inherited adult neuromuscular disease, accounting for 98% of all myotonic dystrophy cases. This is a multi-system disease with major cardiac involvement. Core features are myotonia (delayed muscle relaxation after contraction), progressive weakness and atrophy of the skeletal muscles, cataract, and systemic manifestations, including cardiac involvement [1, 2]. Classical DM1 has been identified as an autosomal dominant disorder associated with the presence of an abnormal expansion of a cytosine-thymine-guanine (CTG trinucleotide) repeat on chromosome 19q13.3 (the DM1 locus). Its incidence is estimated to be one in every 8,000 births annually and its prevalence is estimated at 1/20,000 inhabitants [3–5].

Endomyocardial biopsies and post mortem studies performed on patients with DM1 have documented various degrees of non-specific changes, such as interstitial fibrosis, fatty infiltration, hypertrophy of cardiomyocytes, and focal myocarditis. A selective and extensive impairment of the conduction system is the commonest finding [6]. Respiratory failure and cardiovascular disease are the most prevalent causes of death, accounting for about 40% and 30% of fatalities, respectively [7, 8].

The hypothesis that cardiac arrhythmias may be the most prevalent cause of sudden death in DM1 patients is supported by the absence of other causes of sudden death found at autopsies [6].

Sudden cardiac death may be caused by cardiac arrest, ventricular tachycardia (VT) with degeneration in ventricular fibrillation (VF) or progression to complete AV block [9, 10]. Conduction system abnormalities are commonly observed in DM1. Any part of the conduction system can be affected, but the intraventricular His-Purkinje system is the most frequently involved. Minor conduction defects are often present in the ECGs of asymptomatic pa-

tients in the early stages of disease. Their progression towards more severe conduction defects may cause shortness of breath, dizziness, fainting, syncope, and sudden death. The rate of progression of the conduction abnormalities is usually slow, but occasionally quick, thus making the clinical course of individual patients unpredictable [7]. Delayed impulse propagation along the conduction system can be associated with a long PR interval and/or with a wide QRS complex. Delayed myocardial activation in DM1 is not a consequence of inhomogeneous conduction through scattered areas of fibrosis, but rather of delayed activation along the intraventricular His-Purkinje system [7, 9, 11].

Groh et al. [12], in 406 adult patients with genetically confirmed DM1, showed severe abnormalities on the ECG: no sinus rhythm, PR interval and QRS duration prolongation (≥ 240 ms and ≥ 120 ms, respectively), or second or third-degree AV block. A diagnosis of atrial tachyarrhythmia was an independent risk factor for sudden death. During the follow-up, 20% of the patients died, with one in three of the deaths being sudden.

A careful cardiac evaluation including basal ECG, 24 hour Holter monitoring and echocardiogram should be routinely performed in all patients presenting with DM1. A history of fainting, palpitation, shortness of breath, presyncope or syncope should be carefully researched by interviewing not only the patient but also his or her relatives. Asymptomatic AV conduction delay, in particular in the presence of a prolonged HV interval, represents one of the major therapeutic challenges in DM1, as data on the rate of progression to complete AV block is contradictory. On the basis of nonrandomized observations, some investigators have recommended pacemaker implantation for patients with DM1 and asymptomatic cardiac conduction abnormalities [9, 13].

Conclusions

Patients with DM1 are at high risk of severe cardiovascular events, including sudden death. ECG abnormalities could potentially help predict them. Prophylactic pacemaker implantation in DM1 patients who are identified as being at risk of sudden death according to Groh's criteria [12] reduces the incidence of sudden death. However, pacemaker implantation cannot entirely forestall this event once VTs/VF are involved in the sudden deaths of DM1 patients. In such cases, an implantable cardiac defibrillator could be indicated.

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