Pacing for conduction disturbances in Steinert's disease: a new indication for biventricular ICD?

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Cardiac involvement in classical Steinert muscular dystrophy (dystrophia myotonica, MD1) is characterised by atrial arrhythmias, AV conduction disturbance, ventricular arrhythmias and heart failure. In MD1 patients complaints of fatigue and reduced exercise tolerance are well explained by the muscular weakness, but the same symptoms can be attributed to arrhythmia, atrioventricular block and heart failure. As cardiac pathology is often encountered in MD1 patients, an ECG, echocardiogram and Holter registrations should be performed on a routine basis.
We report on two patients with MD1 who developed Mobitz II block as initial presentation of cardiac disease. (*Neth Heart J* 2006;14:258-62.)

Keywords: myotonic dystrophy, atrioventricular block pacing, atherosclerosis (coronary), heart failure (congestive), cardiomyopathy (dilated), sudden death

Classical myotonic dystrophy (MD), first described by Steinert and called Steinert's disease or MD1, has been identified as an autosomal dominant disorder associated with the presence of an abnormal expression of a cytosine-thymine-guanine (CTG) trinucleotide repeat on chromosome 19q13.3.[1,2] The classical symptoms are myotonia, muscle atrophy, cataract, a characteristic facial appearance and cardiac conduction disturbances. Although the impairment of muscular function is the most obvious symptom for the patient, cardiac involvement is common. The most frequent cardiovascular manifestations are syncope, arrhythmias, atrioventricular block, congestive heart failure and sudden death.[3]

Syncope may occur due to atrial flutter with 1:1 atrioventricular conduction, ventricular tachycardia and complete atrioventricular (AV) block.[4-6] Cardiac involvement predominantly affects the conduction system, while myocardial contractile function is less commonly impaired in MD patients.[7]

Atrial arrhythmias in MD1 are characterised by the low voltage of the P waves, atrial fibrillation (AF) and electrical and functional atrial standstill. The conduction in MD1 is impaired at different levels. First but not the most prominent is the sinoauricular conduction disturbance. AV conduction delay is more rapidly recognised on the surface ECG. Also the distal conduction is impaired, usually in the form of a left bundle branch block (LBBB).

Heart failure is rare in MD1 and often occurs late in the course of the disease. The clinical recognition of heart failure in muscular disease is more difficult than in patients with a normal muscular function as fatigue is inherent to the muscular weakness and exercise tolerance is already impaired by the muscular disease itself.

Case reports

Case 1

A 54-year-old patient with genetically proven Steinert disease MD1 was referred to the outpatient clinic for cardiac evaluation in 2001. He was symptom-free except for general fatigue and muscular weakness. He had no complaints of palpitations or syncope. Physical appearance showed typical facial signs of DM1 with axial, semi-distal and distal compartments involved, causing hanging upper and lower eyelids and hanging musculature of the face with loss of expression.

His ECG showed typical low-voltage P waves of short duration (60 msec), a prolonged PR interval and an LBBB-like QRS complex (figure 1). The echocardiogram showed a normal left ventricular function.

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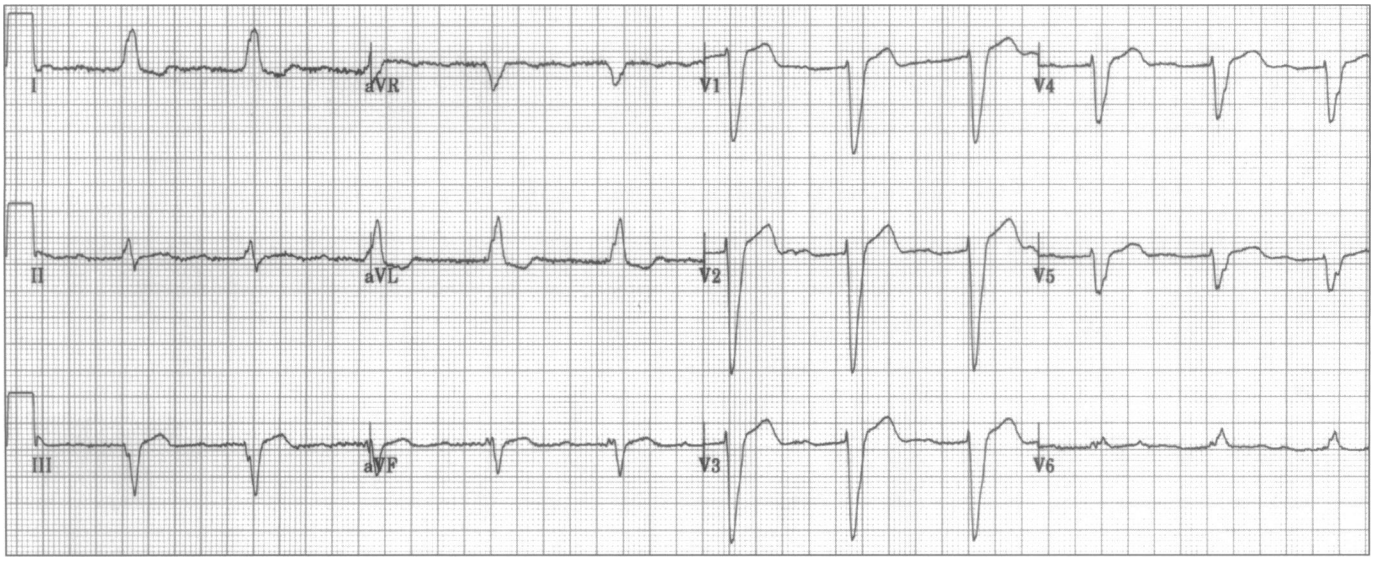

Figure 1. ECG from patient 1 showing low-voltage P waves, prolonged PR segment and left bundle branch like QRS complex.

One year later, the AV conduction progressively deteriorated and Mobitz II was seen on the Holter recording. A DDDR pacemaker was implanted with an atrial lead in the atrial appendage and a ventricular lead in the outflow tract. Again a year later, during routine follow-up, AF was recorded on the ECG. As the AF was symptom-free, and rate control was established by the pacemaker, only acenocoumarol was prescribed. Echocardiographic re-evaluation showed less favourable results as the left ventricular end-diastolic diameter (LVEDD) had increased from 50 mm to 57 mm and LV systolic contraction pattern was overall diminished. The quality of the echo did not allow for proper ejection fraction (EF) measurement. No physical signs of heart failure were present.

Case 2

A 61-year-old male Caucasian, normotensive, former amateur boxer was admitted because of a limited non-Q-wave lateral myocardial infarction complicated by ventricular fibrillation. He was successfully defibrillated in the ambulance. On arrival his blood pressure was 90/60 mmHg and his pulse rate was regular at 80 beats/min. The neurological examination was normal.

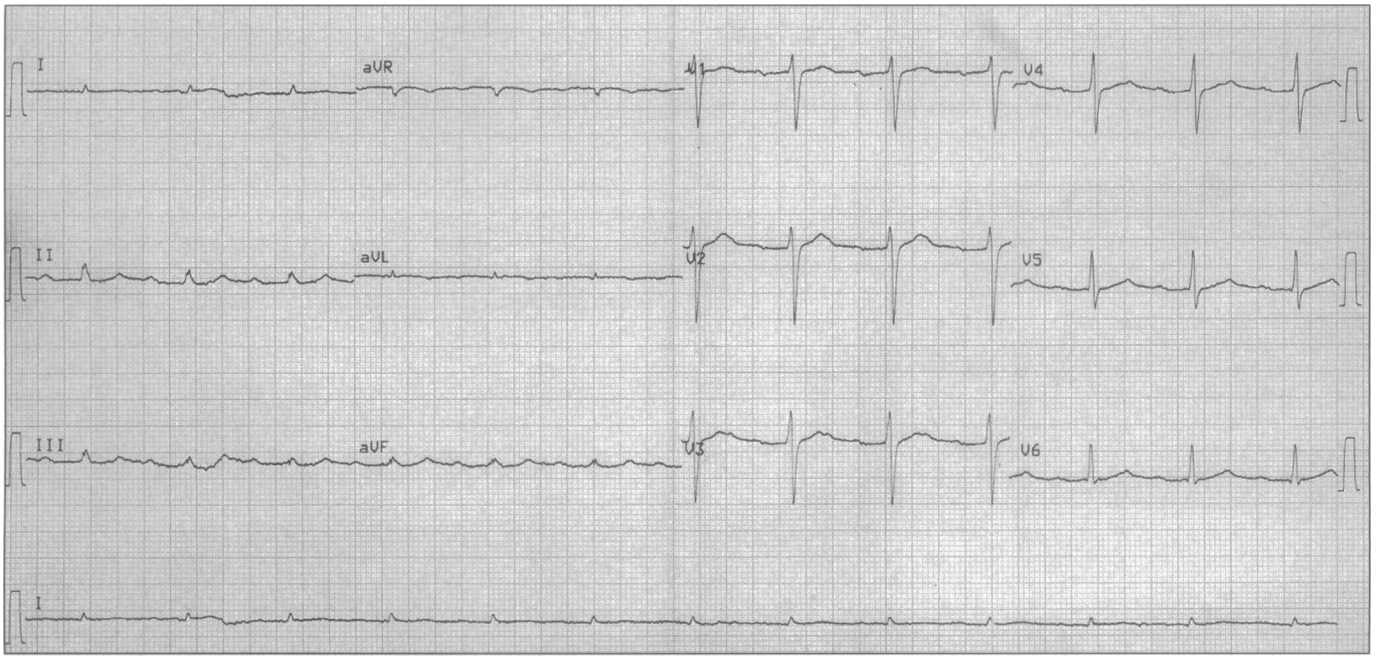

Figure 2. A 12-lead routine ECG from patient 2 showed microvoltage in the standard leads and first-degree AV block.

Serum enzyme concentrations were consistent with minimal myocardial damage (creatine kinase (CK) 1402 U/l, CK-MB 9%, aspartate aminotransferase 170 U/l and lactate dehydrogenase 957 U/l). He was treated with intravenous streptokinase followed by unfractionated heparin and nitroglycerin intravenous drip. An ECG showed diffuse intraventricular (IV) conduction disturbance with low voltage in the standard leads and first-degree AV block. The QRS duration was prolonged, 122 ms, as was the QTc interval, 457 ms (figure 2). MD had been diagnosed in the patient's son (at the age of 30 years) three years earlier. At that time, genetic evaluation of the father (current patient) subsequently revealed the presence of short cytosine-thymine-guanine triplet repeats (36<n<100) on chromosome 19, although electromyography showed no evidence of MD. He had a somewhat sagging facial expression and showed the typical frontal baldness commonly found in MD (figure 3). This was consistent with a minimal form of MD in the father of a patient with the classical adult-onset form of the disease. Determination of the CTG repeat was as described before by Jansen et al.[8] with minor modification. There was a mild dyslipidaemia (total cholesterol 6.4, high-density lipoprotein (HDL) 0.8, low-density lipoprotein (LDL) 4.6, triglycerides 2.28 mmol/l and cholesterol/HDL ratio 8). A previous ECG taken a few years earlier for preoperative screening purposes demonstrated first-degree AV block. During hospital admission, although his MI remained limited, he developed Mobitz II and total AV block with bradycardia varying from 30 to 60 beats/min (figure 4). A dual-chamber pacemaker was implanted.

The pacemaker was programmed to DDD mode with a lower rate of 60 beats/min and upper rate of 140 beats/min. Interrogation of the pacemaker revealed 85% ventricular pacing at follow-up; this was because of a slow intrinsic rhythm. The radionuclide LVEF was 0.15 with global left ventricular hypokinesia. Echocardiography showed a dilated and diffusely hypokinetic left ventricle, mild mitral regurgitation and mildly dilated left atrium. The LVEDD was slightly enlarged at 62 mm (normal 35 to 57). The patient was discharged on acenocoumarol and 2.5 mg enalapril twice daily.

He was readmitted six weeks later because of heart failure. He was discharged on captopril 6.25 mg twice daily, bumetanide 5 mg, ascal 100 mg, isosorbide mononitrate 25 mg, diltiazem CR 120 mg twice daily and fluvastatine 20 mg. Another six months later he was readmitted to the hospital because of progressive angina pectoris, which was initially treated medically. Coronary arteriography demonstrated normal anatomy with a discrete 90% diameter stenosis of the left circumflex artery (LCx) with globally impaired left ventricular function and mild mitral regurgitation. Percutaneous transluminal coronary angioplasty (PTCA) of the LCx was successfully performed.

Six years after the initial event, he was admitted to the hospital for observation of gastrointestinal bleeding. Unwitnessed he died suddenly in-hospital few days later; permission for autopsy was not granted.

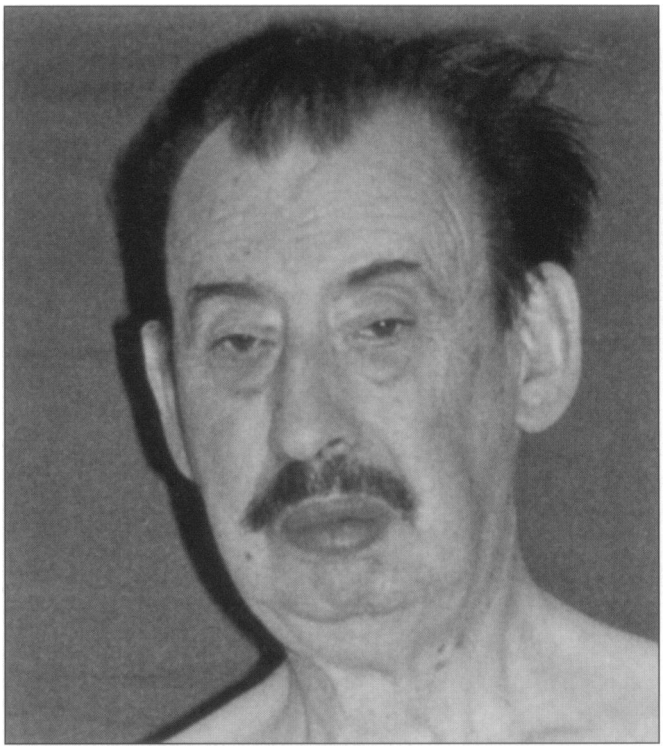

Figure 3. Photograph of patient 2 demonstrating the flaccid attitude and typical facial appearance and deeply receding hairline on both sides of the head, characteristic of myotonic dystrophy.

Discussion

The gene causing classical myotonic dystrophy (Steinert's disease or MD1) is located on chromosome 19q13.3 (MD1 locus) and the locus of the less common disorder MD2 is found on chromosome

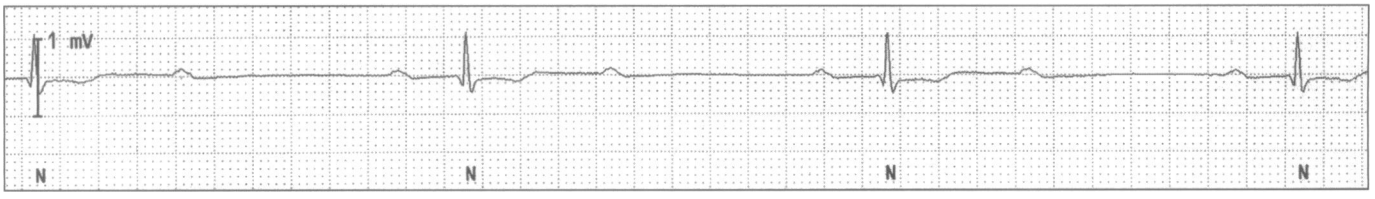

Figure 4. A rhythm strip depicting sinus rhythm with first-degree AV block and Mobitz II block.

3q21 (MD2 locus).[1] Myotonic dystrophy is a genetic disease and although it derives its name from the involvement of skeletal muscle it affects many other organs. Cardiac involvement is quite common and presents as atrial arrhythmias, AV-conduction delay and block. Autopsy usually shows a moderate to severe degree of myocardial fibrosis and in pathology studies on cardiac involvement a slowly progressive dilatation of the ventricles is found.[1] However, severely dilated cardiomyopathy is rare.

In the second case, there is a discrepancy between the limited MI and the catastrophic clinical course. It is unlikely that atherosclerotic changes of the small circumflex artery alone can be held responsible for such severe deterioration, although the myocardial infarction might have initiated or triggered a deleterious disease process.

The conduction system is always more extensively affected than the contractile myocardium and high-grade AV block requiring pacemaker therapy is a well-known complication of the disease. In our patients, a dual-chamber pacemaker was implanted. Intraventricular conduction dispersion is believed to be the cause of the high incidence of sudden cardiac death, which is the cause of death in 15 to 30% of the patients. The typical ECG of MD1 patients depicts complete LBBB (5 to 25%) with first-degree AV block (20 to 40%), as was found in case 1.[1] But the ECG in our second case demonstrated first-degree AV block without diffuse intraventricular conduction delay. Cardiac involvement has also been documented in other muscular dystrophy such as Becker, Duchenne, Emery-Dreifuss and limb-girdle muscular dystrophy (LGMD).[9,10]

It has also been reported that life-threatening cardiac dysrhythmias and conduction disturbances occur in the newly recognised LGMD necessitating pacemaker therapy.[10] Recent reports have shown a high incidence of sudden death in individuals with lamin A/C mutations with or without permanent pacemakers.[11] In a pooled meta-analysis of all previously published cases of lamin A/C mutations, Van Berlo et al. reported that sudden cardiac death was the most frequent (46%) cause of death even after permanent pacemaker therapy. Based on these findings ICD therapy may be suggested as a new indication in LGMD patients treated with pacemakers to prevent sudden cardiac death.[12]

Our patients had had first-degree AV block long before the onset of disease manifestations. When they developed a conduction defect, it rapidly deteriorated into Mobitz II and complete AV block. After pacemaker implantation, dilated cardiomyopathy developed with episodes of congestive heart failure in case 2. As it can be appreciated from our cases, first-degree AV block is suggested to be an early sign of cardiac involvement and occasionally it may be the only apparent cardiac disorder.[2] Early dilated cardiomyopathy may have been silently present, but our second patient was completely asymptomatic. Impaired exercise tolerance in muscular dystrophy patients is a very late symptom of heart failure as vigorous exercise with a concomitant circulatory burden is not possible due to the impaired skeletal muscular function. On the other hand, fatigue is a normal finding in muscular dystrophy, and not readily recognised as a symptom of heart failure.

It has been documented that patients with MD1 were more likely to have conduction abnormalities (52%) and wall motion dysfunction (28%).[7,13] Abnormalities of the conduction system frequently require permanent pacing therapy,[6] whereas overt signs of congestive heart failure are rarely reported[14,15] but dilated cardiomyopathy has been infrequently observed in MD.[16] In case 2, the condition deteriorated significantly after the limited MI. Ischaemic changes and fibrosis may have triggered or facilitated the occurrence of ventricular arrhythmias. Fatty infiltration has been reported in the most severely diseased subjects and has frequently been associated with the presence of more advanced conduction disturbances.[2] In case 2, the cardiac involvement had serious consequences for the course of his illness. In view of the extensive involvement of the conduction system, some dilatation of the left ventricle was to be expected, but the ejection fraction was severely depressed (15%). Progression of the dilated cardiomyopathy is usually slow in myotonic dystrophy; therefore ACE inhibitor and/or β-blocking therapy might be indicated in the course of the disease.

Future directions?

Both patients were treated with a permanent DDDR pacing system. But this strategy could not protect the second patient from sudden death. Ventricular arrhythmias are common in MD1 patients. Spontaneous episodes of both monomorphic and polymorphic ventricular tachycardia and even fibrillation have been consistently reported.[17] The progressive deterioration of the left ventricular function, the progression of AV conduction disturbances and the occurrence of ventricular tachyarrhythmia poses the question whether a biventricular ICD should be the management of choice if a pacemaker is indicated.

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