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Myotonic dystrophy type 1 and high ventricular vulnerability at the electrophysiological evaluation: ICD yes or not?

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A significant number of sudden death (SD) is observed in myotonic dystrophy (DM1) despite pacemaker implantation and some consider the ICD to be the preferential device in patients with conduction disease. According to the latest guidelines, prophylactic ICD implantation in patients with neuromuscular disorder should follow the same recommendations of non-ischemic dilated cardiomyopathy, being reasonable when pacing is needed. We here report a case of DM1 patient who underwent ICD implantation even in the absence of conduction disturbances on ECG and ventricular dysfunction/fibrosis at cardiac magnetic resonance. The occurrence of syncope, non-sustained ventricular tachycardias at 24-Holter ECG monitoring and a family history of SD resulted associated with ventricular fibrillation inducibility at electrophysiological study, favouring ICD implantation. On our advice, DM1 patient with this association of SD risk factors should be targeted for ICD implantation.

Key words: implantable cardioverter defibrillator, myotonic dystrophy type 1, sudden death

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Conflict of interest
The Authors declare no conflict of interest

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Introduction

Myotonic dystrophy type 1 (DM1) is the most frequent muscular dystrophy in adults. Cardiac involvement is reported in about 80% of cases, even in asymptomatic patients [1]. Conduction system disturbances on surface ECG or ventricular dysfunction are considered the most relevant risk factors for sudden cardiac death (SD), favouring pacemaker (PM) implantation according to latest guidelines [2,3]. However, recent data showed that SD, striking up to one third of patients, can also occur for ventricular tachyarrhythmias (VTA) and that other predictive factors like syncope, family history of SD or non-sustained VT should be taken into account for risk stratification [4]. We report the case of a mildly symptomatic DM1 patient who underwent ICD implantation for high ventricular vulnerability at the electrophysiological evaluation even in the absence of either conduction disturbances at ECG or ventricular dysfunction/fibrosis at non-invasive evaluation by echocardiogram and cardiac magnetic resonance.

Case report

A 42 year-old woman, affected by poorly symptomatic DM1 presented at our emergency department for syncope and palpitations. She was diag-

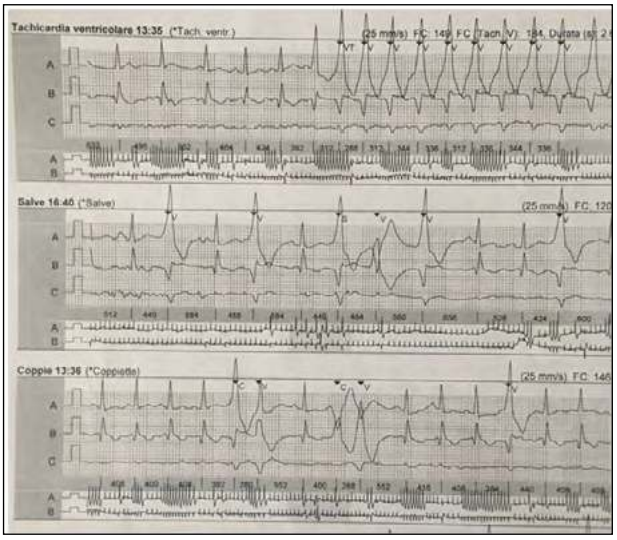

Figure 1. NSVT at 24 hour Holter ECG recording.

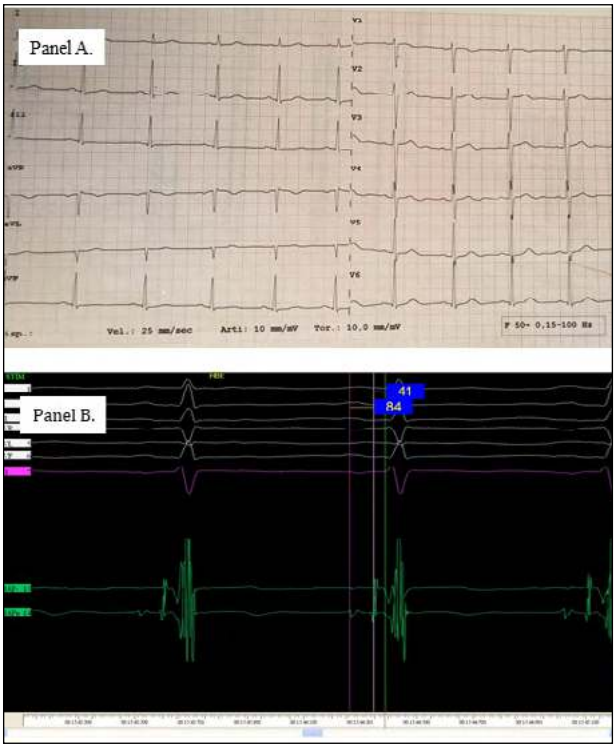

Figure 2. Panel A. basal ECG-Panel B. HV interval at electrophysiological study.

nosed with DM1 three years earlier showing an increased CTG repeat length, with a number size defined between 50-500. The patient showed temporal muscle atrophy, proximal weakness at lower limbs and grip and evoked myotonia. Needle electromyography (EMG) showed mild myopathic changes and myotonic discharges. The patient reported a case of SD in her family history (maternal grandmother, at age 29). On arrival at our department the vital signs were the following: blood pressure 110/70 mmHg, peripheral oxygen saturation 99% in room air, heart rate 70 bpm. No specific drugs were assumed. Basal surface ECG showed sinus rhythm with a PR interval of 0.16 seconds and a QRS duration of 0.10 seconds. A recent 24 hours-Holter ECG monitoring recorded 27 episodes of non-sustained VTs (Fig. 1). Echocardiography showed preserved left ventricular (LV) systolic and diastolic function (EF 55%). Cardiac magnetic resonance (CMR) excluded intramyocardial fibrosis and confirmed a preserved biventricular systolic function. Electrophysiological study (EPS) showed normal correct sinus node recovery time (CSNRT 420 msec) and atrio-ventricular node conduction times (AH 84 msec; HV 41 msec) (Fig. 2). During ventricular stimulation from right ventricle apex (refractory period: 200 msec with drive of 600 msec), sustained ventricular fibrillation (VF) was easily induced (coupling intervals: 600-240-200 msec) and rapidly interrupted with single external DC-Shock. EPS was followed by dual chamber transvenous ICD implantation. ICD remote home monitoring (Medtronic CareLink® System) was provided for VTAs burden surveillance. Low dosage of bisoprolol was started with rapid relief from palpitation and dizziness. ACE-inhibitors were not started for hypotension. Patient was regularly discharged on 7th day from admission. At 1 year of follow up, the patient was still asymptomatic on bisoprolol, and in good clinical conditions. Remote monitoring showed VTAs monthly burden of 0.4%.

Discussion

Myotonic Dystrophy type 1 is an autosomal, dominant disorder due to CTG expansion in the untranslated 3' region of the DM1 protein kinase (DMPK) gene and is the most frequent muscular dystrophy in adults [1]. Cardiac involvement often precedes the muscular/neurological signs and up to one third of deaths is sudden and unexpected, showing that risk stratification is crucial in the management of DM1 [2]. SCD is most likely due to high-degree atrioventricular (AV) block; however, ventricular tachyarrhythmias are increasingly recognised as a common finding in these patients and might explain some cases of sudden death after pacemaker (PM) implantation [5]. Paroxysmal supraventricular tachyarrhythmias (atrial fibrillation, atrial flutter, atrial tachycardia) are a common finding on electrocardiographic monitoring with a prevalence up to 25% in DM1 patients. Atrial fibrillation/flutter (AF/AFl), a frequent feature in DM1 patients, may be the first clinical manifestation of the disease in

young patients and seems to increase the mortality in this population.[6] Given the high risk of supraventricular arrhythmias and their consequences, clinical and instrumental strategies for reducing the risk of atrial fibrillation are of pivotal importance in the optimization of clinical management.

Previous studies showed that abnormalities of the conduction system on surface ECG (PR interval > 240 msec, QRS interval > 120 msec, left bundle branch block) were independent risk factors for SD, presumably owing to the progression of conduction system disease to a complete atrio-ventricular block [5]. Currently, a HV interval > 70 msec at EPS is predictive of an appropriate indication for PM implantation in DM1 [7]. However, a significant number of SD is observed, despite the PM implantation, and some clinicians consider ICD as the preferential device for DM1 patients with conduction disease [8,9]. Myocardial fibrosis at CMR is present in 40% of DM1 patients and is not predicted by ECG, ECG-Holter monitoring and echocardiography, but is often associated with increased risk of SD [10]. According to the latest guidelines, the prophylactic implantation of ICD in patients with neuromuscular disorders should follow the same criteria as in non-ischemic dilated cardiomyopathy, so an ICD implantation may be reasonable in DM1 patients when pacing is needed [2]. However, in DM1, VTAs may occur even in patients with normal ECG and preserved LV systolic function. A recent large study on 1388 DM1 patients reported a 3.6% cumulative incidence of SD over a median 10-year follow-up, with the involvement of multiple mechanisms including conduction defects, sustained VTAs and extracardiac causes [4]. According to this study, age, male sex, syncope, heart rate and 1st degree AV block were independent predictors of overall mortality, at a multivariate analysis. Of note, age, family history of SD and left bundle brunch block were significantly associated with SD. Furthermore, non-sustained VTAs, recorded at Holter ECG monitoring, were the only predictors of sustained VTAs [4].

We describe the case of a young woman affected by early stage DM1 – with preserved cardiac function and absence of conduction abnormalities either at basal surface ECG or EPS evaluation – who needed ICD implantation for the presence of syncope, non-sustained VTAs at 24-Hour ECG monitoring, and a family history of SD associated with a VF inducibility at EPS. The decision for ICD implantation was in accordance with ESC Syncope Guidelines. The high ventricular vulnerability was not associated with intramyocardial scar or cardiac dysfunction at CMR. In our view, further studies are needed and a revision of current recommendations for ICD implantation in DM1 could be considered, mostly in patients presenting with syncope, non-sustained VTAs and a family history of SD. In this subset of patients, the evidence of high ventricular vulnerability at EPS, rather than cardiac dysfunction or conduction abnormalities, would be useful in identifying subjects eligible for ICD implantation to prevent unexpected deaths, whose incidence is not negligible. In conclusion, to date, the best strategy for SD risk stratification in DM1 patients is not yet well known. In addition to Groh criteria (PR ≥ 240 ms, QRS ≥ 120 ms or atrial tachy-arrhythmias), recent evidences showed that age, syncope, family history of SCD and left bundle branch block are independent predictors of SD. Nevertheless, the role of ICD implantation in DM1 patients with preserved systolic function is not fully clarified and the choice of best device to implant is based on patient-centred electrophysiological evaluation. Our clinical case confirms the recommendations that family history of SD, syncope with palpitation and non-sustained VTAs may be considered red flags for high risk of SD in DM1 patients, even when conduction disorders, ventricular dysfunction and CMR ventricular fibrosis cannot be detected with conventional instrumental investigation. This risk is confirmed by the high ventricular vulnerability at the EPS evaluation in these patients. Further studies are needed to evaluate if the EPS-guided therapy, including the prophylactic ICD implantation in inducible patients, will prevent SD in DM1 patients without ventricular dysfunction and conduction disorders compared with conventional therapy.

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