

Manuscript Details

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Article type	Case report

Abstract

In myotonic dystrophy (MD), tissue degeneration affects not only the skeletal, but the cardiac muscle, too. In one third of the patients the cause of death is of cardiac origin. We report on our patient's case, who was diagnosed with type 1 MD at the age of 52, in whom episodes of critical bradycardia with first-degree of atrioventricular block was detected, resulting in a pacemaker implantation. Invasive cardiac electrophysiologic study (EPS) was performed, during which ventricular fibrillation was registered. A shock electrode was added to the previously implanted pacemaker, enabling defibrillation in case of detection of a sustained ventricular arrhythmia. As of August 2018, 22 episodes of sustained ventricular tachycardia were identified, with the device successfully terminating the malignant arrhythmias. Our case shows that EPS and the succeeding implantation of an implantable cardiac defibrillator is highly important in identifying and terminating ventricular arrhythmias in high risk MD patients.

Keywords myotonic dystrophy, cardiac electrophysiologic study, risk stratification, implantable cardioverter defibrillator

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To Prof. Victor Dubowitz
UCL GOS Inst. of Child Health
Dubowitz Neuromuscular Centre
London, England, UK

Dear Editor-in-Chief,

Enclosed we submit our manuscript entitled “*Successful termination of multiple malignant ventricular arrhythmias with implantable cardioverter defibrillator in a patient with myotonic dystrophy*”, which we are submitting for publication in the ***Neuromuscular Disorders***.

In our article, we report on our patient’s case, who was diagnosed with type 1 myotonic dystrophy, underwent invasive cardiac electrophysiologic study, where ventricular fibrillation was registered thus implantable cardioverter defibrillator was implanted. 1 year after the implantation, anti-tachycardia pacing maneuvers (20 cases) and adequate defibrillation shocks (2 episodes) restored sinus rhythm, as the device successfully terminated the malignant arrhythmias.

The manuscript is not under consideration elsewhere and none of the paper's contents have been previously published. All the authors have read and approved the final manuscript of the original article, and all of them contributed significantly to the design, analysis or critical revision of the data.

All authors declare no conflict of interest.

We are submitting the manuscript with the understanding that if it is accepted for publication, copyright in the article, including the right to reproduce the article to all forms and media, shall be assigned exclusively to the Publisher.

Looking forward to hearing from you soon.

Sincerely yours,

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In myotonic dystrophy tissue degeneration affects the cardiac muscle as well.

In one third of the patients the cause of death is of cardiac origin.

Invasive cardiac electrophysiologic study for risk stratification is important.

Implantation of a cardiac defibrillator is crucial in high risk patients.

Successful termination of multiple malignant ventricular arrhythmias with implantable cardioverter defibrillator in a patient with myotonic dystrophy

– a case report –

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Abstract

In myotonic dystrophy (MD), tissue degeneration affects not only the skeletal, but the cardiac muscle, too. In one third of the patients the cause of death is of cardiac origin. We report on our patient's case, who was diagnosed with type 1 MD at the age of 52, in whom episodes of critical bradycardia with first-degree of atrioventricular block was detected, resulting in a pacemaker implantation. Invasive cardiac electrophysiologic study (EPS) was performed, during which ventricular fibrillation was registered. A shock electrode was added to the previously implanted pacemaker, enabling defibrillation in case of detection of a sustained ventricular arrhythmia. As of August 2018, 22 episodes of sustained ventricular tachycardia were identified, with the device successfully terminating the malignant arrhythmias. Our case shows that EPS and the succeeding implantation of an implantable cardiac defibrillator is highly important in identifying and terminating ventricular arrhythmias in high risk MD patients.

Introduction

Myotonic dystrophy (MD) is a multisystemic, autosomal dominant muscle disease, affecting mostly the adult population with a prevalence of 0.5-18.1:100.000. (1) Tissue degeneration affects not only the skeletal, but the cardiac muscle as well, which acts as an important factor in the decreased life expectancy in patients with MD: in one third of the patients the cause of death is of cardiac origin. (2–4) The most common cardiac manifestations are arrhythmias and conduction disorders, caused by the dystrophic rearrangement of cardiac muscle tissue, affecting the integrity of the pacemaker and conduction systems. To define the level of the possible cardiac involvement, cardiology work up is of particular importance in patients with known MD. (5) We report on a case of our patient with type 1 MD, in whom the thorough cardiology risk estimation and accordingly, the subsequent implantation of a cardioverter defibrillator (ICD) proved to terminate several periods of malignant cardiac arrhythmias.

Case report

The 62-year old female patient presented with difficulties of gait started at the age of 52. Neurological physical examination revealed moderate weakness of the proximal muscles associated with a severe weakness of foot dorsiflexion, the later was being responsible for gait difficulties. Hypotrophy of the leg muscles, as well as marked grip myotonia was detected. Electromyography (EMG) identified myopathy and myotonic discharges with a distal predominance, while electroneuronography (ENG) was normal. Biopsy of the left quadriceps muscle demonstrated dystrophic changes. Laboratory tests were unremarkable, including normal TSH and insulin levels, but creatine kinase (CK) was moderately elevated (3x normal). The diagnosis of type 1 myotonic dystrophy was verified by genetic testing. Episodes of critical bradycardia with first-degree of atrioventricular block with 264 ms PR interval could be

registered one year after the initial diagnosis. Echocardiography showed normal ejection fraction with mild concentric left ventricular hypertrophy. No signs of any insufficiency in the coronary circulation could be identified in the course of the coronary angiography, and thus new onset arrhythmia could not be deemed to be ischemia-related and dual-chamber pacemaker implantation was performed in 2010. There was no evidence of malignant ventricular arrhythmia either before or after the pacemaker implantation. The patient was completely symptom free, control echocardiography examinations showed no changes during the cardiology follow-up. She underwent bilateral cataract surgery at the age of 58. Within the confines of an ongoing prospective study, in June 2017, at the age of 70 she was hospitalized for further cardiac risk stratification by means of invasive cardiac electrophysiology. No abnormalities could be identified in her laboratory parameters. Ventricular fibrillation (VF), resulting in hemodynamic instability and loss of consciousness occurred during catheter positioning of the electrophysiological study even before starting programmed electrophysiological stimulation. Defibrillation was necessary to restore the sinus rhythm. Considering the primary disease and the malignant ventricular arrhythmia during electrophysiologic examination, a shock electrode was added to the previously implanted pacemaker, enabling defibrillation in case of detection of a sustained ventricular arrhythmia. Sustained ventricular tachycardia (VT) (22 episodes) could be identified on the event recorder of the ICD during the cardiologic control examination in August 2018. Anti-tachycardia pacing (ATP) maneuvers (20 cases) and adequate defibrillation shocks (2 episodes) restored sinus rhythm, as the device successfully terminated the malignant arrhythmias. In the following cardiology check-ups till February 2019, no further arrhythmias were detected.

Discussion

MD is the most common adult onset multisystemic muscle disease. (1) In general, the first symptoms appear between the age of 20 and 40 years. Although the most dominantly affected tissue is the skeletal muscle, respiratory, endocrinologic, ophthalmologic, gastrointestinal and cardiologic manifestations can be also present. Two major types of MD can be distinguished. Type 1 (Steinert disease) is caused by an expansion of trinucleotide (CTG) repeat, contained within the 3' untranslated region of the myotonic dystrophy proteinase gene (DMPK) on the 19th chromosome. (6) Presenting with milder symptoms, MD type 2 is caused by the expansion of the CCTG tetranucleotide repeat of the ZNF9 gene on the 3rd chromosome. (7) In both types of diseases the pathological increase of the repeat numbers cause a blockage of the intranuclear messenger (m)RNA processing by binding of the pathologic mRNA to mRNA-binding proteins, thus inhibiting the processing and expression of various proteins, most importantly ion channels, eventually leading to myotonia and conduction disorders. Further significant consequence of the mutation is the insulin resistance due to the involvement of insulin receptor mRNA. The disease has been associated with conduction abnormalities both on the AV-nodal and infra-Hisian tissue. (3) Despite of the considerable size of the patient population, no extensive study and recommendation of the patients' cardiology work up, risk prediction and treatment were conducted until 2015. In a systematic review Lau et al. summarized the data of cardiac problems in patients with MD and provided a practical approach to the management of these patients with a focus on the prevention of complications related to conduction disturbances and arrhythmias. (5) Patients with documented sustained ventricular arrhythmia or significant left ventricular (LV) dysfunction (LV ejection fraction <35%) should be referred for ICD implantation as per standard guidelines. In addition, ICD implantation should be considered in the case of inducibility of VT during invasive electrophysiologic study (EPS). (5) In a registry involving 406 DM1 patients underwent pacemaker or ICD implantation for conduction abnormalities / LV dysfunction, Bhakta et al. reported seven sudden cardiac deaths

in the pacemaker group and concluded that for patients with high risk of VT/VF and sudden cardiac death ICDs should be preferred rather than pacemakers. (8)

Most recently, Russo et al. suggested ICD implantation in DM1 patients with permanent pacing indication and spontaneous or inducible ventricular arrhythmias, even when cardiac function is preserved. (9) In conclusion, our case shows that EPS is a highly important method to identify patients with high risk of ventricular arrhythmias (VT and VF), and the succeeding implantation of an ICD is crucial in the prevention of a malignant arrhythmia-associated cardiac death.

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I, Péter KUPÓ MD (corresponding author) confirm that all co-authors have read and agreed the contents of this manuscript submitted to Neuromuscular Disorders.

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