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CASE REPORT

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Atrial paralysis due to progression of cardiac disease in a patient with Emery-Dreifuss muscular dystrophy

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Abstract

We present the progressive nature of the disease in a 26 year-old woman who had suffered from Emery-Dreifuss muscular dystrophy detected at the age of three. In 2002, at the age of 20, due to recurring presyncopal states accompanied by sinus bradycardia and atrioventricular block, she was implanted with a dual chamber pacing system. During testing of the pacing in 2008, permanent electrical atrial stand-still without atria stimulation were detected and the mode of heart stimulation was changed to VVIR. (Cardiol J 2011; 18, 2: 189–193)

Key words: Emery-Dreifuss muscular dystrophy, atrial paralysis, pacing

Introduction

Emery-Dreifuss muscular dystrophy (EDMD) is a rare disease classically inherited in an X-linked recessive fashion. It is characterized by: early contractures of the elbow and posterior cervical muscles with joint stiffening and dislocation, progressive muscle weakness beginning in childhood, atrophy primarily in humeroperoneal muscles, and cardiac involvement. Muscular dystrophy manifests itself in the patient in relatively benign changes in the muscular system, such as contracture of the elbow and ankle joints with weakening of the limb muscles which, to some extent, affect motor ability.

Although female carriers of the disease do not show the full spectrum of symptoms, they may develop cardiac conduction system defects [1].

Arrhythmias and dilated cardiomyopathy are the major manifestations of cardiac disease in the course of EDMD. Abnormalities in impulse generation and conduction are relatively frequent. Typical disorders of the electrophysiological properties include: the first type of atrioventricular block progressing to the second and third type of block, supraventricular rhythm disorders, atrial electrical silence as well as ventricular rhythm disorders which may be malignant and lead to sudden death. Frequently, permanent pacing is required for symptomatic bradycardia or heart block [2].

Case report

The case presented is of a 26 year-old woman who had EDMD detected at the age of three. The patient's father suffered from dilated cardiomyopathy and, following implantation of a heart pacemaker, died suddenly at the age of 32.

The patient has been under cardiac observation since the age of 12. Early electrographic (ECG) Holter monitoring performed between 1994 and 2000 did not show significant sinus bradycardia. However, over the years, there was some progression in supraventricular disorders of heart rhythm. Episodes of atrial fibrillation and flutter became more frequent and lasted longer. At first, only single premature ventricular beats were observed. In

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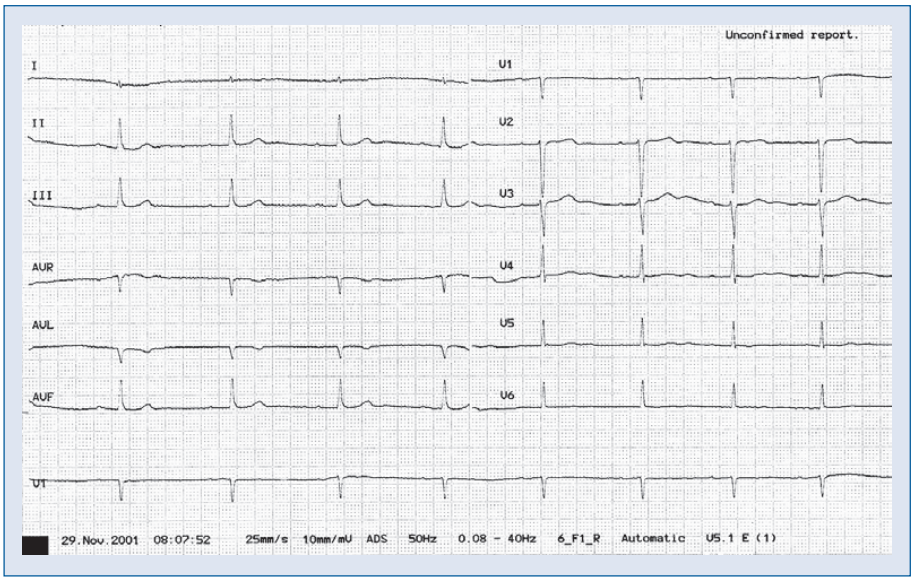

Figure 1. Sinus bradycardia 51 bpm, small amplitude and short duration (0.04 s) of P-waves, first-degree atrioventricular block.

2000, during a 24-hour ECG recording, pairs of ventricular beats were recorded, together with one episode of ventricular tachycardia comprising 12 beats.

In 2002, at the age of 20, the patient suffered from recurring presyncopal states. Standard and 24-hour ECG readings showed sinus bradycardia 45–56 bpm, with first-degree atrioventricular block, and supraventricular rhythm disorders, especially episodes of atrial fibrillation and flutter. What was striking was the small amplitude and short duration of P-waves (Fig. 1). Echocardiography recordings showed normal heart structures with proper left ventricular systolic and diastolic function. Due to symptomatic sinus bradycardia, disorders in atrioventricular conduction with first degree block type, the patient with EDMD had a two-chamber stimulation system implanted, functioning in DDDR mode [3]. Additionally, 100 mg/day of metoprolole was administered.

In the years 2002–2008, the patient's condition was satisfactory. There were no occurrences of syncope or symptomatic tachyarrhythmia. The heart stimulation system, functioning in DDD mode, was used to its full capacity.

During one of the most recent examinations of the stimulation system, there was no atria stimulation detected, despite the maximum energy of the stimulating impulse. The stimulation of ventricles was correct and there was no significant change in the level of stimulation. After switching off the stimulation system, an atrioventricular junctional rhythm of 35–40 bpm was observed (Fig. 2). At the same time, zero potential from the right auricle of the heart was recorded, which could attest to a permanent electrical atrial stand-still. Other parameters of the stimulator did not change significantly and remained at acceptable values. Radiological examination did not show any change in the location of the atrial electrode. The echocardiography examination, compared to earlier recordings, revealed dilatation of both atria (Fig. 3) without hemodynamic function (lack of 'A' wave in the Doppler mitral flow pattern).

Due to the lack of effective atrial stimulation, the mode of heart stimulation was changed to VVIR. The patient remains under constant cardiac care with periodic echocardiography examination of the heart and the progression of rhythm disorders (24--hour ECG monitoring), which may influence further decisions as to the possible implantation of a cardioverter-defibrillator (ICD) in order to prevent sudden cardiac death.

Discussion

Emery-Dreifuss is a primary muscular, genetically conditioned disease. It is most frequently inherited in an X-linked recessive fashion, although occasionally it may take the autosomal dominant form. The gene responsible for X-linked EDMD is emerine, located in chromosome Xq28 [4]. Muscular defect is primary in comparison to the changes

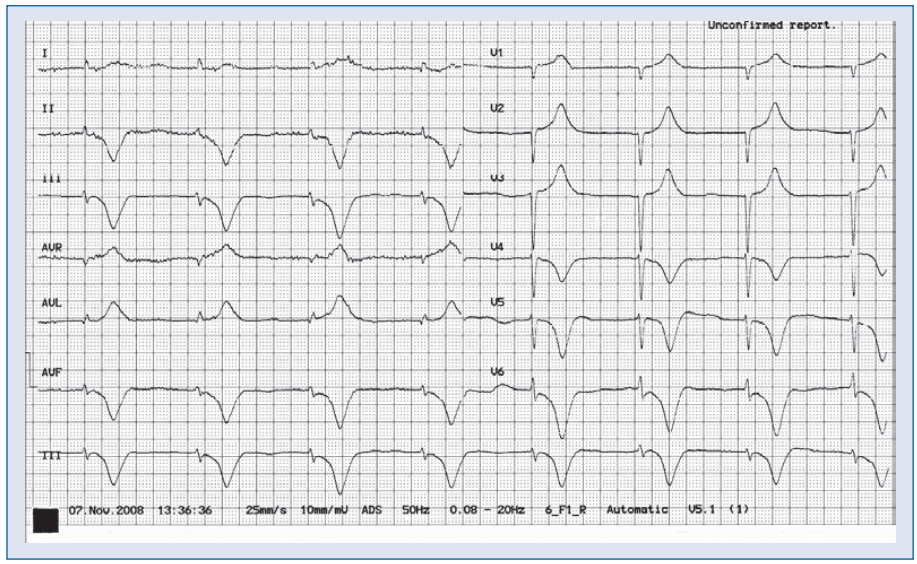

Figure 2. Atrioventricular junctional rhythm 44 bpm, P-waves are missing.

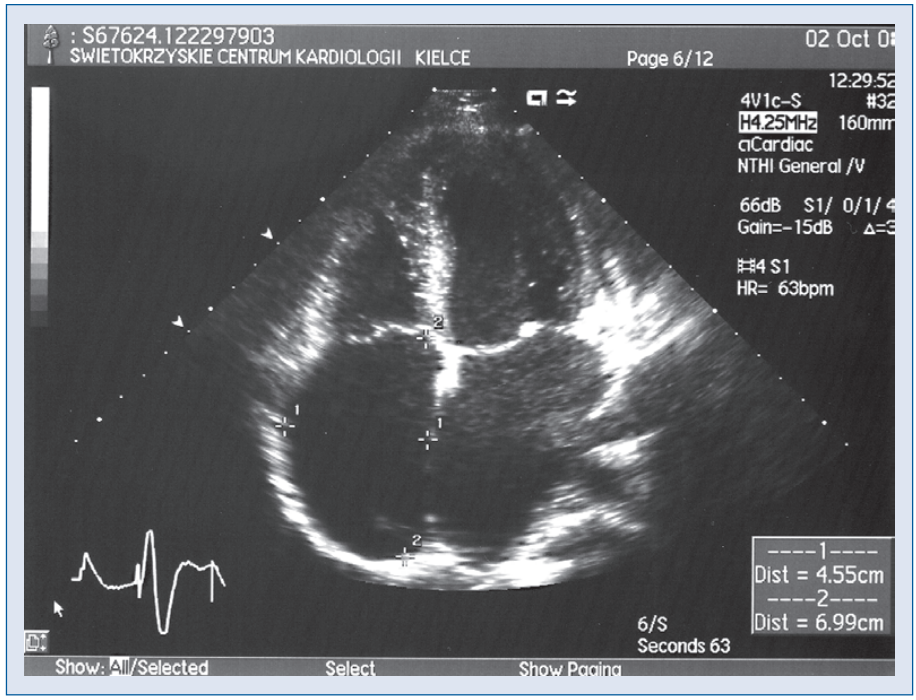

Figure 3. Echocardiography examination: apical four chamber view, atrial enlargement.

taking place in the nerve endings of dystrophic muscles, which are secondary. EDMD has its onset between the ages of three and six. Among the earliest features of this disorder are contractures in elbow and ankle joints, as well as slowly progressive perineal, brachial and scapular muscle weakness. There is no muscle hypertrophy and no weakness of facial muscles. Deep movements are usually suppressed. Mental development is good [5].

The activity of phosphorylase kinase in blood serum is usually slightly increased. Muscle fibre necrosis is diagnosed by muscle biopsy and the proliferation of the connective tissue in *endomyosium*. Immunofluorescence tests detect the presence of

emerine at the nuclear membrane of muscle cells and skin specimens [4, 5].

The clinical course varies and depends mostly on two factors: weakening of muscle strength and organ complications, such as disorders of the heart rhythm and conductivity [4, 5]. In this type of dystrophy, heart disorders are manifested in various conductivity disorders: from the prolongation of P-Q interval to atrial paralysis, atrial mechanical and electrical silence, left anterior bundle branch block, QRS prolongation, complete heart block with sudden cardiac death, which can be prevented by the implantation of a pacemaker or prophylactic ICD placement [6–8].

In classic cases, atrioventricular first degree block progressing to third degree block takes place in the second or third decade of life [2]. ECG changes detect the disease in the heart muscle, the conduction system of the heart on various levels, and the vessels that supply it. Both autopsy and myocardial biopsies detect fibrosis, fatty degeneration and atrophy of nodal tissue, atrioventricular node tissue, His bundle and its branches [9].

Common rhythm disorders include: additional junctional beat, sinus bradycardia, paroxysmal supraventricular tachycardia, atrial fibrillation and fluttering and ventricular tachycardia [10]. Ventricular rhythm disorders may be a cause of sudden death. There are also cases with detected prolonged QT interval and torsade de pointes ventricular tachycardia [11]. The causes of ventricular arrhythmia vary and may be connected to the presence of late ventricular potentials and slow conductivity of ventricular muscles [12]. An additional pro-arrhythmic factor is low coronary reserve present in asymptomatic patients with normal left ventricle function. Additionally, dystrophic and myotonic changes in tissue cells of the heart muscle may lead to disorders of systolic and diastolic function and indirectly cause arrhythmia [13]. In patients suffering from muscular dystrophy, there might also be tachycardia coming from His bundle branches. This mechanism is present in symptomatic patients with tachycardia with broad QRS complexes [14]. Heart complications which cause sudden death may occur even in asymptomatic patients suffering from muscular dystrophy.

In 1999, based on previous results, Lazarus et al. [2] proposed an algorithm for the treatment of patients suffering from muscular dystrophy. The algorithm comprises electrophysiological examination when there are symptoms which might be connected with rhythm or conductivity disorders, even with normal ECG results. The implantation of a pacemaker was recommended in patients with conventional indications as well as in asymptomatic patients, although with the prolongation of conductivity in His bundle to 70 ms. According to European Society of Cardiology guidelines of 2007 [15], the implantation of a pacemaker is recommended for patients with muscular dystrophy in the presence of third degree atrioventricular block and second degree Mobitz I and II types (class I of the guidelines). The implantation may be considered for patients with first degree atrioventricular block (class IIb of the guidelines). The implantation of a pacemaker is also recommended in the case of any block of His bundle branch (class IIa of the guidelines).

In comparison with Duchenne muscular dystrophy, EDMD progresses slowly and benignly. However, heart disorders constitute a serious problem. In our patient, the occupation of skeletal muscles was typical: contractions of elbow and ankle muscles with muscle weakening. Until the age of 20, there was no damage to the heart muscle detected by echocardiography examination. Initially, heart complications were connected with the dysfunction of sinus node with progressing bradycardia and supraventricular rhythm disorders. Due to symptomatic tachy-bradycardia with first degree atrioventricular block, a two-chamber stimulation system was implanted. At first, electrical and mechanical activity was good. However, attention was paid to P-wave morphology of low voltage and short duration which would testify in this case to electrical and mechanical atrial paralysis, which manifested itself six years later.

The patient's father, most probably suffering from EDMD, had the symptoms of dilated cardiomyopathy and died suddenly in spite of the implantation of a heart pacemaker. Dilated cardiomyopathy is more common in patients whose chances of survival have been improved by pacemaker implantation. EDMD is a disease inherited as a recessive chromosome X-linked feature, which makes the disease fully symptomatic in male patients, whereas in female patients not all symptoms are manifested.

The placement of a heart pacemaker is the treatment of choice in progressive damage of the stimulus conduction system in patients with EDMD [2, 6]. It does not protect from the consequences of malignant ventricular arrhythmia. So far, there are no guidelines for the implantation of ICD for primary prevention in patients suffering from muscular dystrophy without echocardiographical features testifying to the damage of left ventricular systolic action. The prognostic value of electrophysiological examination for this group of patients remains un-

known. However, the family history, as well as observed episodes of ventricular tachycardia detected by 24 hour ECG monitoring, and the progressive nature of the disease, constitute factors of potentially unfavourable prognosis. Continuing thorough observation of the patient is required, with the issue of qualifying the patient according to ICD remaining open.

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