Journal of Clinical and Basic Cardiology

An Independent International Scientific Journal

Journal of Clinical and Basic Cardiology 2000; 3 (2), 145-146

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Indexed in
Chemical Abstracts
EMBASE/Excerpta Medica

Krause & Pachernegg GmbH · VERLAG für MEDIZIN und WIRTSCHAFT · A-3003 Gablitz/Austria

Cardiopathy in a Patient with Emery-Dreifuss Muscular Dystrophy

C. Stucki, S. Christen, A. Gerber[1]

We report on a 25 year old man with the rare lesion of X-chromosomal recessive Emery-Dreifuss muscular dystrophy. The clinical picture is characterized by muscle weakness, contractures and progressive cardiopathy. The cardiac disease presents itself as progressive heart failure with dilatation of both atria and ventricles. The patient has pathognomonic atrial standstill, junctional bradycardia of about 40 bpm and cardiac arrests up to 3700 msec. These abnormalities are caused by pathologic changes with replacement of muscular tissue with adipose and fibrous tissue in the atria and ventricles. The patient belongs to a German family with 17 affected males over 3 generations, 9 of whom died suddenly at ages between 37 and 59 years. Whether these sudden deaths occurred due to asystoly or tachyarrhythmia is unknown. Based on his family history and on the progressive cardiopathy our patient received an implantable cardioverter/defibrillator (ICD) with an integrated VVIR pacemaker. Furthermore, medication with ACE-inhibitors and warfarin has been started. *J Clin Basic Cardiol 2000; 3: 145–6.*

Key words: Emery-Dreifuss, conduction disturbances, atrial standstill, cardiomyopathy

Emery-Dreifuss muscular dystrophy (EMD) was first described in 1961 by Dreifuss and Hogan. [1] It is a rare X-linked recessive disease characterized by variable slowly progressive muscle wasting and weakness, early contractures of the elbows, Achilles tendons and postcervical muscles. Cardiac manifestations are often severe, including dilated cardiomyopathy, complete heart block and sudden death. Until the report of Emery and Dreifuss in 1966 the cardiac manifestations were not recognized. [2] Later the gene was found to be located in the Xq28 region. Atrial arrhythmia that often progress to atrial standstill with bradycardia are the pathognomonic, unusual electrophysiological disorder in the disease. In symptomatic patients pacemaker implantation due to bradycardia is an accepted therapy although risk of sudden death in young adulthood remains very high. [3, 4]

Case report

A 25 year old man with the diagnosis of EMD was admitted to our hospital because of palpitations and dizziness. During the past year he had complained of gradually progressive exertional dyspnoea and fatigue. He denied a history of angina or syncope. He is a member of a known family with EMD living in lower Bavaria (Germany), described by Rotthauwe in 1972. [5] In this family, 9 of 17 affected males died suddenly at ages between 37 and 59 years, and several of them had advanced cardiomyopathy. His motor and mental development was not delayed. The disability of a mild muscular weakness in the upper arms, shoulders and lower legs, as well as contractures of elbows started in early childhood. There had been no progression of the motor disability since he was a teenager.

Physical examination on admission showed contractures at the elbows and muscle wasting in the shoulder girdle, biceps and leg (calf and dorsiflexors) muscles. The blood pressure was 125/75 mmHg and the heart rate was regular at 44 beats/minute (bpm). Jugular venous pressure was at the sternal angle without hepatojugular reflux. Auscultation revealed a 2/6 holosystolic murmur along the lower left sternal margin without any radiation. Lung auscultation was normal. In the laboratory tests, serum creatine phosphokinase level was elevated to 1493 units per litre (< 270 units per litre in normal subjects). A twelve-lead ECG showed no evidence of a p-wave in any lead. There was a junctional rhythm with a ventricular rate of 40 bpm. There were no T-wave changes (Figure 1). Holter monitoring showed a minimal heart rate of 35 bpm, but neither sinus pauses longer than 2000 ms nor ventricular arrhythmia were registered. Maximal heart rate was 91 bpm. An event recording study during 7 days showed several asymptomatic cardiac arrests of up to 3700 msec duration and one episode of bradycardia at a rate of 28 bpm. In a bicycle exercise test the patient achieved 210 Watt in steady

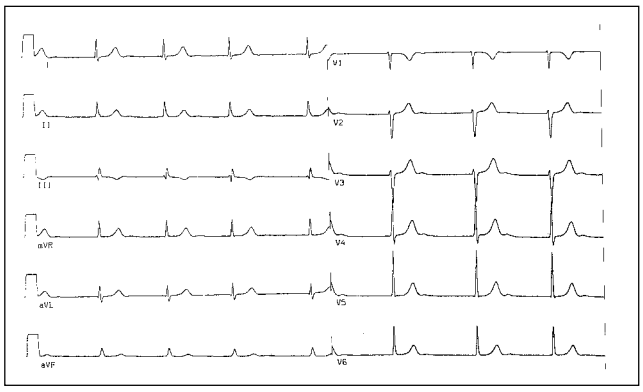

Figure 1. Twelve-lead electrocardiogram demonstrating absence of atrial activity, junctional rhythm and bradycardia at a rate of 40 beats per minute

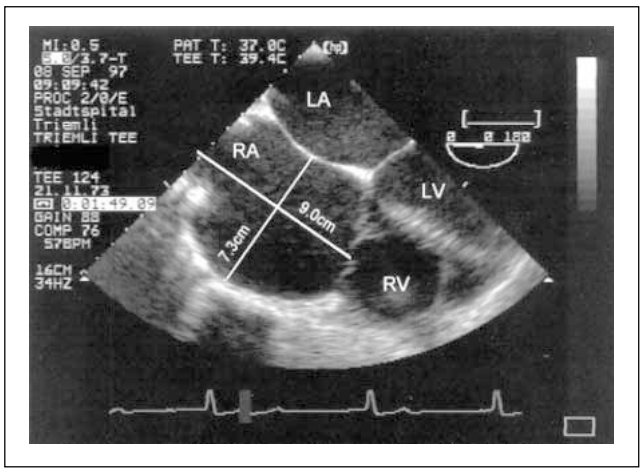

Figure 2. Transesophageal echocardiogram showing a grossly dilated right atrium and a moderately dilated left atrium without any active contraction

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state (expected 230 Watt), the ventricular frequency reached a maximum of 126 bpm. Blood pressure increased from 140/100 mmHg to 220/120 mmHg. Some single premature ventricular beats and ventricular bigeminus were registered during the exercise. A transthoracic and transesophageal echocardiogram showed a grossly dilated right atrium (area 60 cm^2 from apical view, normal < 19 cm^2) and a moderately dilated left atrium (area 33 cm^2, normal < 23 cm^2) without any active contraction (Figure 2). The right ventricle showed a moderate dilatation (54 mm short axis from apical, normal < 42 mm). Left ventricle showed slight concentric hypertrophy (LV-mass-index 154 g/m^2 BSA, normal < 137 g/m^2) with diffuse hypokinesis resulting in a mild reduction of the ejection fraction to 45 %.There was mild mitral and severe tricuspid regurgitation upon Doppler examination with normal valve morphology. Tricuspid insufficiency pressure gradient was 30 mmHg, indicating mild pulmonary hypertension. Studies of the respiratory system showed that resting lung function and CO-diffusion were normal. During spiroergometry maximal oxygen uptake was 31.1 ml/kg/min (69.2 % of predicted capacity), maximal respiratory minute volume was 107 l/min (predicted value 214.4 l/min).

In conclusion the patient showed findings pathognomonic of EMD with typical skeletal and myocardial muscular affects. Weakness of intercostal muscles explains the above mentioned decrease of respiratory function. The limiting problem of our patient is the advanced and progressive cardiomyopathy with risk of progressive dilatation, cardioembolic events and syncope or sudden death due to rhythm disorders. We started a therapy with ACE-inhibitors and oral anticoagulation with warfarin. Based on other case reports with sudden deaths despite antibradycardia therapy with pacemakers and based on our patient's family history with an excessive rate of sudden death in young adulthood we decided to implant a prophylactic cardioverter/defibrillator system in combination with a VVIR-pacemaker (ICD). The rate response is an important option, in view of the progressive chronotropic incompetence, which is to be expected in the near future.

During 2 years of follow-up the cardiomyopathy has remained stable and the patient oligosymptomatic without any syncope or shock.

Discussion

Emery-Dreifuss muscular dystrophy (EMD) is a X-chromosomal recessive disease with rather mild involvement of skeletal muscles and progressive cardiopathy, which limits life expectation to medium adulthood. Cardiac findings in the disease are unique. The cardiopathy is characterized by a marked loss of myocardium and its replacement by adipose and fibrous tissue starting in both atria and the conducting system and progressing to both ventricles. This process results in a dilatation of right and later left atrium, proceeding to dilatation of ventricles.

The rhythm disorders begin with a decrease and finally the loss of the p-wave in the ECG in childhood and progressive atrio-ventricular block with slow junctional rhythm. [6]

Electrical and mechanical atrial standstill with very thin and pale atrial walls is the pathognomonic finding. The increased risk of systemic embolism is obvious and comparable to the situation in atrial fibrillation. Several cases with either cerebral or peripheral embolic events have been described. [7] The progression to the ventricles leads finally to congestive heart failure and its complications. Death due to terminal heart failure is common but sudden death appears to be more frequent. Whether this occurs due to asystoly or ventricular tachyarrhythmia is unknown. Despite antibradycardia therapy with pacemakers several affected patients have died suddenly. [8]

Our patient is in a progressive phase of the pathognomonic heart disease with dilatation of all four chambers and atrial standstill, left ventricular dysfunction, secondary mitral and tricuspid regurgitation due to dilatation of the annulus. He has a junctional rhythm with 40 beats per minute (bpm) and had several asymptomatic pauses up to 3700 msec and bradyarrhythmias down to 28 bpm. Worldwide about twenty families exist with EMD, and some single cases have also been described. [7, 8] Our patient is member of a known family with 17 males affected with EMD in 3 generations. Nine of them died suddenly and five other have had partial or complete atrioventricular block.

Permanent ventricular pacing improves symptoms and prolongs the life span in patients with sinus bradycardia, sinus pause or heart block. [3, 8] Because of the complete loss of myocardium in the atria, atrial pacing is not of aid. Therefore, in view of the chronotropic incompetence and its expected progression, our patient received a ventricular pacing system with a rate response option. [9] Little is known about the aetiology of fatal accidents in these patients. About 40 % of EMD patients died suddenly, many of them without preceding cardiac symptoms. [10] Whether the risk of sudden death bases on asystoly or on tachyarrhythmias seems to be unknown. [5]

This fact and the excessively high sudden death rate in our patient's family gave us the indication for implantation of a prophylactic cardioverter and defibrillator in combination with the VVIR-pacemaker. To reduce the cardiac remodeling, ACE inhibitor therapy was started, in view of its therapeutic effects in dilated cardiomyopathy of any aetiology. The importance of prophylactic long-term oral anticoagulation for the prevention of systemic embolism originating from the dilated and still standing left atrium is obvious.

During two years of follow-up the patient has remained stable and oligosymptomatic.

The ICD has not been activated yet.

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