HEART & LUNG

Case Studies in Cardiopulmonary Disorders

Restrictive cardiomyopathy as a cardiac manifestation of myofibrillar myopathy

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ABSTRACT

Objectives: Restrictive cardiomyopathy (RCM) has been repeatedly reported as a cardiac manifestation of certain neuromuscular disorders, but only in single patients with myofibrillar myopathy (MFMP).

Case Report: In a 19-year-old woman with a history of short stature, tiptoe-walking since childhood, fixed joint contractures, severe scoliosis requiring surgical correction, elevated levels of creatine kinase, and RCM, MFMP was diagnosed based on her clinical presentation, her elevated muscle enzymes and a muscle biopsy. An electrocardiogram showed an atrioventricular-block I, paroxysmal sinus-tachycardia, biphasic P-waves, right-axis deviation, abnormal repolarization, and episodes of supraventricular tachycardia. Echocardiography confirmed her RCM. Her respiratory function was markedly reduced, despite surgical correction of her severe scoliosis at age 14 years. After an aggravation of heart failure because of atrial flutter, the patient profited from successful cardioversion and diuretics.

Conclusion: Electrocardiographic abnormalities such as atrial flutter and RCM represent cardiac manifestations of MFMP. Cardioversion can be successful, and oral anticoagulation may prevent cardioembolic events.

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Although restrictive cardiomyopathy (RCM) has been repeatedly reported as a cardiac manifestation of certain neuromuscular disorders (NMDs),[1,2] it has been observed only in single patients with myofibrillar myopathy (MFMP).[3-7]

Case Report

The patient is a 19-year-old white woman, with a height of 154 cm and a weight of 47 kg, with a history of tiptoe walking since early childhood, contractures of the elbow and knee joints, and exertional dyspnea and scoliosis since age 10 years. RCM, exercise intolerance, and elevated levels of serum creatine-kinase were first detected at age 12 years. A muscle biopsy from the vastus lateralis muscle at age 12 years led to a diagnosis of a reducing body myopathy with secondary mitochondrial abnormalities. An analysis of her muscle mitochondrial DNA revealed a 3-kb deletion with a heteroplasmy rate of 4%, which was not detectable in blood lymphocytes. At age 14 years, she

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underwent surgical correction of her scoliosis, with a marked improvement of cardiac and pulmonary functions within 1 year after surgery. Preoperative investigations revealed normal coronary angiography and systolic function. An endomyocardial biopsy revealed hypertrophic cardiomyocytes, enlarged nuclei, vacuolated cytoplasm, an increase in interstitial fibrous tissue, perivascular infiltrates of histiocytes, and edema. Since age 15 years, the patient became increasingly exercise-intolerant and developed exertional dyspnea. At age 18 years, an atrioventricular-block I and echocardiographic signs of myocardial thickening were recorded for the first time. Right and left heart catheterization disclosed values for the right atrium of 11/9/7 mm Hg, for the right ventricle of 39/2/5 mm Hg, for the pulmonary artery of 25/14/18 mm Hg, for the pulmonary capillary wedge of 20/12/17 mm Hg, for the aorta of 79/55/66 mm Hg, and for the left ventricle of 81/10/17 mm Hg. Spiroergometry revealed a ventilatory capacity reduced to 52% of normal, with a maximal lactate increase to 3 mmol/L. Stress testing revealed a reduction of maximal physical capacity to 46 Watt. Cardiac therapy had included captopril, acetylsalicylic acid, and furosemide, alternatively with spironolactone, since age 12 years. Sildenafil, given at age 18 years for 6 months because of suspected pulmonary hypertension, had to be discontinued because of pulmonary complaints and a deterioration of her cardiac status.

At age 19 years, the patient requested a reevaluation because of uncertainty about her cardiac and neurological diagnosis, and because of increasing exercise intolerance, exertional dyspnea, and easy fatigability. A clinical cardiologic investigation produced normal results. An electrocardiogram (ECG) indicated an AV-block I, a biphasic P-wave, right-axis deviation, and repolarization abnormalities. A 24-hour ECG revealed 5 nonsymptomatic episodes of supraventricular tachycardia for up to 15 seconds each, and 1 episode of sinus tachycardia. Echocardiography confirmed the diagnosis of RCM (Figure 1), but did not find myocardial thickening. Spirometry revealed severely reduced respiratory function, to about 50% of normal. Because of a resting heart rate in the upper normal range, bisoprolol at 1.25 mg/day was initiated, but was not tolerated because of arterial hypotension. Thus digitoxin was prescribed, resulting in a normalization of her heart rate. Six months later, her condition deteriorated. She underwent episodes of vomiting, gained 2 kg of weight, and developed peripheral edema. An ECG showed an atrial flutter, with a ventricular rate of 50 to 70 beats per minute (Figure 2). Oral anticoagulation was initiated. Three weeks later, electrical cardioversion restored her sinus rhythm, and this was associated with marked clinical improvement. As of her most recent follow-up, she was no longer receiving digitoxin, instead taking spironolactone (50 mg/day), furosemide (40 mg/day), and phenprocoumon. She reported occasional irregular heartbeats for several hours, which disappeared spontaneously on every occasion.

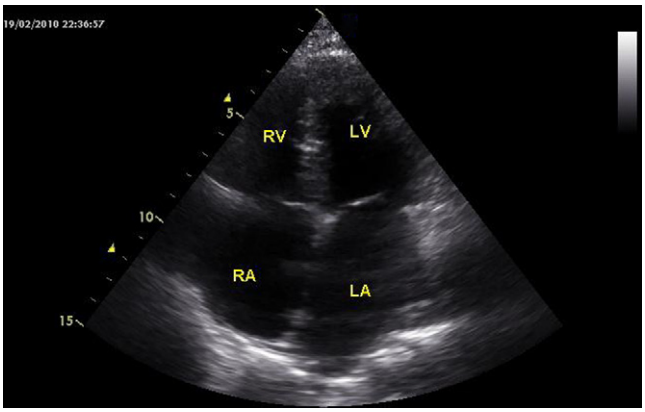

Figure 1 – Echocardiography (apical 4-chamber view) shows enlarged right atrium (RA) and left atrium (LA), but normal-sized and contracting left ventricle (LV) and right ventricle (RV).

A clinical neurologic examination at age 19 years indicated scoliosis, a deformity of the thorax, contractures of the elbows and small finger joints and knees, but normal muscle strength, normal muscle volume, and preserved tendon reflexes. Blood chemical investigations revealed creatine kinase at 755 U/L (normal range, <145 U/L), myoglobin at 189 μg/L (normal range, <64 μg/L), aldolase at 15.1 U/L (normal range, <7.6 U/L), slightly elevated glutamate-oxalat transaminase, glutamate-pyruvate transaminase, and lactate-dehydrogenase, and pro-brain-natriuretic peptide at 1676 pg/mL (normal range, <125 pg/mL). A second muscle biopsy from the right lateral vastus muscle showed severe myopathic changes, with indications for MFMP (Figure 3). A molecular genetic workup for mutations in the desmin gene, however, was negative.

Discussion

Our patient is interesting in terms of her MFMP in combination with RCM and atrial flutter, and her favorable response to cardioversion. An atrial flutter was reported in a single patient with RCM,[8] but that patient did not suffer from any NMD. More frequently than with atrial flutter, RCM is associated with atrial fibrillation. RCM is a rare form of cardiomyopathy, characterized by a bilaterally enlarged atria, normal-sized left and right ventricles, and a restrictive filling pattern on Doppler sonography, with a deceleration time <150 milliseconds in the transmitral flow. RCM is either idiopathic or a manifestation of cardiac involvement in systemic disease, including NMDs. Reports of hereditary NMDs with RCM have included autosomal-dominant MFMP, Emery-Dreifuss muscular dystrophy attributable to lamin A/C mutations, mitochondrial myopathy, multicore myopathy, and distal myopathy with rimmed vacuoles.[2] Secondary myopathies with RCM include