Acute Myocardial Injury in a Child with Duchenne Muscular Dystrophy: Pulse Steroid Therapy?

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ABSTRACT

Heart implication in Duchenne muscular dystrophy usually is present in the form of dilated cardiomyopathy, manifested as heart failure and arrhythmias. To delay progression, including heart deterioration, prednisone is recommended as preventive treatment. We report the case of an 11-year-old boy diagnosed with Duchenne muscular dystrophy at the age of seven, who was on preventive treatment with oral prednisone (0.75 mg/kg/day) and beta blocker (metoprolol, 1 mg/kg/day). Suddenly, the patient presented acute chest pain, vomiting and sweating. The electrocardiogram showed ST elevation in inferior leads. Troponin T was increased to 30814 pg/ml (normal values <14 pg/mL). The echocardiography revealed reduced contractility of the posteroinferior wall of the left ventricle. After excluding coronary implications by coronary angiography, we increased the oral prednisone to 1.4 mg/kg/day for five days and added enalapril (0.5 mg/kg/day, po). The response was positive, with a rapid decrease of the troponin T value to 3186 pg/mL in five days and gradual recovery of myocardial contractility afterwards.

Keywords: acute myocardial injury, Duchenne muscular dystrophy, oral pulse steroid therapy.

INTRODUCTION

Duchenne disease is known as a hereditary myopathy which affects as well the heart muscle. Cardiac damage occurs slowly, most often in the form of dilated cardiomyopathy (1), and is manifested as heart failure and arrhythmias. To delay the onset and progression of cardiac disorders, corticosteroid treatment is recommended, with the effect of a lower all-cause mortality rate, and a significant reduction in heart failure related deaths (2).

Acute deterioration of the cardiac function in Duchenne muscular dystrophy (DMD) is anecdotic in the medical...
literature. Previously reported cases showed mostly asymptomatic clinical onsets, discovered by routine evaluation, in which the evolution was spontaneously favourable (3-5).

CASE REPORT

A 11-year-old boy was referred from a county hospital for acute treatment in a presumed case of ST-segment elevation myocardial infarction (STEMI). He was hospitalized locally with a 12 hours’ onset of a typical anginal retrosternal pain, nausea, vomiting and sweating. The chest pain lasted for one hour and was followed by short recurrent episodes. It was a typical angina pain with irradiation on the left arm, accompanied by vegetative manifestations. On arrival, he was receiving aspirin and enoxaparin.

At the age of seven, he was diagnosed with progressive DMD, and he was under treatment with prednisone (0.75 mg/kg/day) and metoprolol (1 mg/kg/day). He had a family history of a maternal cousin (boy) who died at the age of 20. His neurological development was normal up to the age of 7, when he started to manifest gait disturbances, difficulties when climbing stairs, followed by muscle fatigue. He had a mild mental retardation; he had started to talk at the age of four and was diagnosed with autism.

Clinical examination revealed an overweight boy (45 kg, BMI 24.72 kg/m², > 95th percentile), in good clinical condition, afebrile, with normal pulmonary breath sounds and tachycardia (heart rate 95/min under beta blocker treatment), 3rd heart sound present, and BP 90/65 mmHg. He had significant muscular weakness of the limbs; he was experiencing difficulty in walking and was mostly kept in a wheelchair.

Biological investigations performed at admission objectified: leukocytosis, 17930/mm³ with increased neutrophils (70%), mild inflammatory syndrome, CRP 24.8 mg/L; LDH 1996 U/L, AST 149 U/L, ALT 149 U/L, troponin T 30814 pg/mL (normal values <14 pg/mL), CK 18482 U/L and CKMB 763 U/L were found to be elevated, suggestive of acute myocardial necrosis.

At admission, ECG changes were noted: ST segment elevation, necrotic Q wave in inferior leads (DII, DIII, aVF) (Figure 1).

Echocardiography highlighted reduced contractility of the left ventricle posteroinferior wall, with an ejection fraction of 45%.

The severe onset mimicking an acute myocardial infarction raised the suspicion of a possible coronary obstruction, and we performed a coronary angiography (Figure 2), which showed normal epicardial coronary arteries.

We also excluded other possible causes for myocardial necrosis with patent coronary arte-
ries and ST segment elevation. Thus, myocarditis was excluded by negative serology parameters (enterovirus, adenovirus, parvovirus B19, cytomegalovirus, human herpes virus, and Epstein-Barr virus) and by cardiac magnetic resonance imaging (CMR) evaluation. CMR showed myocardial fibrosis localized in the posteroinferior wall consistent with the ECG and echocardiography changes and absence of myocardial inflammation.

Consequently, we stopped both the antiplatelet and anticoagulant treatment. We increased the dose of prednisone to 60 mg/day for five days (oral pulse steroid therapy), and returned to the dose of 30 mg/day. The levels of enzymes decreased after the oral pulse therapy to AST 42 U/L, CK 1500 U/L CKMB 54 U/L, and troponin T 3186 pg/mL.

Enalapril (1 mg/kg/day), furosemide (1 mg/kg/day) and spironolactone (1 mg/kg/day), and carvedilol (0.5 mg/kg/day) afterwards, completed the treatment.

**DISCUSSION**

Duchenne disease is a genetic disease transmitted by the X chromosome and caused by a mutation at the level of the dystrophin gene, which also affects the heart. This gene suffers a mutation and the production of dystrophin is lost, generating muscular destruction. Dystrophin has the characteristic of stabilizing the membrane, but in its absence the cell membrane collapses and some ruptures may appear with exteriorization of the cell enzymes. With time, muscular tissue is exchanged with fat and fibrotic tissue without contractile properties (6). For the heart, this will generate cardiomyopathy, systolic dysfunction, and arrhythmias. A slow onset pattern for cardiac impairment and deterioration is generally described for these patients (6-8).

Regarding the acute onset of the symptoms, there are only a few reports in literature describing an acute onset of the cardiac involvement in DMD mimicking an acute myocardial infarction. One paper described a 12-year-old boy with asymptomatic Duchenne, who was discovered with acute necrosis by electrocardiographic signs of ST segment elevation and compatible enzyme dynamics (5). Two others publications reported about a 10-year-old boy with DMD who manifested symptoms of acute myocardial infarction during severe physical exertion (4) and a 13-year-old boy with signs of acute myocardial infarction (3). Neither a diagnostic algorithm, nor a therapeutic schema for acute onset is known.

For acute phase diagnosis, like in this case, we believe that coronary artery imaging is required, and for the periodic evaluation of disease progression, CMR may be useful. Gadolinium-enhanced CMR may reflect myocardial damage and fibrosis and can provide a better quantification of the left ventricle dimensions and function (1). There are characteristic changes in the CMR aspect of DMD patients. The fibrosis process begins in the left ventricle, posterobasal segment (2) or basal inferolateral (9) and may imply the whole myocardium in an advanced form of disease. Gadolinium-enhancement CMR is a very sensitive method which can be applied early in DMD patients in order to support the initiation of the cardioprotective treatment (1) but also to the DMD carrier’s patients (9).

For the acute phase, in the medical literature, there is no indication for steroid therapy administered as pulse therapy. But various studies regarding the chronic use of steroids in DMD patients showed a 76% lower mortality rate by reducing the heart failure-related deaths and a 62% lower rate of new-onset cardiomyopathy (10). Animal studies showed that steroid use (combined with ACE inhibitors as well as single use) had a protective effect on the heart in long term administration (1). Also, carvedilol and inotropic treatment in combination with ACE-inhibitors improve the left ventricular systolic function in patients with muscular dystrophy (11). Analyzing all these data, oral steroid pulse therapy for five days concomitant with IECA administration was recommended. Diuretic treatment was intended to prevent volume overload, a side-effect associated with steroid therapy.

Our report emphasizes the role of the oral pulse steroid therapy in stabilizing the membrane of the cardiac myocytes in the situation of an acute injury which was not reported in previous cases. Steroids are demonstrated to be the only medication which slows the muscular decline and reduce the long-term all-cause mortality, including cardiac mortality in DMD patients. The recommended regimen of administration is prednisone 0.75 mg/kg/day. Doses less than 0.3 mg/kg/day did not have any effect, and those higher than 1.5 mg/kg/day were not more effec-
tive. In Europe, prednisolone and deflazacort may be used as well (7, 8).

After five days of 60 mg oral prednisone application (1.4 mg/kg/day), our patients’ T troponin level decreased from a maximum of 30810 pg/mL to 3186 pg/mL, and the myocardial contractility started to gradually recover. Prednisone was reduced from 1.4 mg/kg/day to 0.75 mg/kg/day, and by the 10th day, the level of the T troponin decreased to 318 pg/mL.

The particularity of this case consists of the appearance of an acute coronary syndrome in a patient with known DMD. In any acute coronary syndrome in adults, the treatment usually includes antiplatelet and anticoagulant therapy as well as revascularization therapies, which are not normally needed in the DMD pathophysiology. The only proven effective long-term treatment in DMD patients is steroid therapy both on muscle weakness and decline of muscle strength and function (7, 8), including preservation of cardiopulmonary function (12). We applied this treatment, adjusting doses as for oral steroid pulse therapy, to stop and prevent acute severe muscular destruction. Oral pulse therapy with prednisone was efficient in this case of acute myocardial necrosis.

**CONCLUSION**

In Duchenne muscular dystrophy, cardiac changes usually appear in form of dilated cardiomyopathy, but seldom can mimic an acute myocardial infarction. In absence of vascular obstruction, a steroid pulse therapy was efficient in the case of acute myocardial necrosis. Corticosteroids, which are typically used to slow down the cardiac deterioration in chronic administration, may be administrated in acute severe cases as a pulse therapy in an attempt to stabilize the cardiac cellular membrane.


**REFERENCES**