CARDIAC COMPLICATIONS IN DUCHENNE MUSCULAR DYSTROPHY IN CHILDREN

Ioana Grigore[1], Mariana Frasin[2], Georgeta Diaconu[1]

[1]Pediatric Neurology Clinic, "Sf. Maria" Emergency Clinical Hospital for Children, Iasi

[2]Functional exploration laboratory, "Sf. Maria" Emergency Clinical Hospital for Children, Iasi

ABSTRACT

Cardiac complications are frequently diagnosed in Duchenne muscular dystrophy (DMD), clinical manifestations generally appear after age 10. ECG recordings objectified various changes in these patients, the most common being represented by extensive R waves in V1, left deep Q waves, conduction abnormalities and arrhythmias. Echocardiographic examination may objective the presence of subclinical cardiac dysfunction in children under 12 years old diagnosed with DMD. In patients where standard echocardiographic examination is normal, myocardial performance index is a parameter useful in early detection of asymptomatic cardiac abnormalities. Cardiovascular magnetic resonance provides information both on left ventricular systolic function and myocardial tissue changes and occurrence of fibrosis, lesions rarely objectified before the age of 10 years. All these explorations should be considered in children with DMD at the end of a complete neurological exam.

Keywords: cardiac manifestations, Duchenne muscular dystrophy, child

Progressive muscular dystrophies include a heterogeneous group of disorders characterized by primitive, progressive muscle degeneration genetically determined. Duchenne muscular dystrophy is the most common and most serious of these disorders with an incidence of 1 in 3500 newborns (Santos, 2010). Duchenne muscular dystrophy (DMD) is transmitted X-linked and is caused by the absence of dystrophin, the responsible gene that was identified in 1986 and is located on the short arm of chromosome Xp21 (Kunkel 1986, Monaco 1986).

Dystrophin normally plays an important role in stabilizing the cellular membrane both skeletal muscle and cardiac myocytes and it's absence results fragility of the sarcolemma and degeneration of muscle fibers (Menke, 1995). Pasternak (1995) noted that the decrease or absence of dystrophin causes atrophic changes at the level of muscle fiber which is dependent of the degree of deficit.

Clinically DMD is characterized by progressive decrease in muscle strength initially proximal, with worsening of motor deficit in the second and third childhood. The patients lose of ambulation by the age of 10-12 when the child requires wheelchair. Evolution of the disease is progressive, in time being affected all skeletal, respiratory and heart muscles and gastrointestinal smooth muscle.

Recent studies have reported a 90% incidence of cardiac changes at pediatric age patients with DMD (Holmgren, 2003; Connuck, 2008). Asymptomatic cardiac involvement has been reported in 25% of children younger than 6 years and in 60% children aged 6 to 10 years (Bushby, 2003; Finsterer, 2003). McNally (2007) believes that nearly all patients with DMD who reach the third decade of life, present cardiomyopathy, but frequently diagnosis are delayed because physical inactivity of the patients masks the symptoms of heart failure. Clinical manifestations become obvious after the age of 10 years, being present in all DMD patients older than 18 years (Bushby, 2003; Finsterer, 2003). The presence at the clinical examination of some minor signs as sinus tachycardia may suggest early cardiac damage (Gulati, 2005), but usually clinical signs of cardiomyopathy appear late.

DMD associated cardiomyopathy may be considered a form of "heart dystrophy" characterized

Corresponding author:
Ioana Grigore, "Sf. Maria" Emergency Clinical Hospital for Children, 62 V. Lupu Street, Iasi
E-mail: ioanag74@yahoo.com

by impaired of architecture of myocardial cells secondary fibrosis. According to studies by nuclear magnetic resonance myocardial fibrosis is initially located at the basal-posterior and lateral wall of the left ventricle (Silva, 2007; Puchalski, 2009), the consequence being the reduction of contractile force and the disturbance of the electrical activity of myocardial cells.

Electrocardiographic changes in children with Duchenne muscular dystrophy

Electrocardiograms (ECG) have objectified in children with DMD various changes (Fig. 1, Fig. 2), the most frequently changes being represented by:

- tall R wave in V1-V2;
- deep Q wave in V5-V6;
- conduction disturbances;
- arrhythmias.

James and all (2011) considers that ECG abnormalities are common in young children diagnosed with DMD. Also they consider that heart damage is present before the onset of motor symptoms. The authors electrocardiographically analyzed 78 children under 6 years with DMD and identified ECG changes in 78% of these cases, the most common being those due to left ventricular impairment.

In a study containing a group of 131 patients with a mean age of 9 years 4 months, diagnosed with DMD, Santos and all (2010) analyzed the ECG to highlight possible changes associated with cardiac progressive muscle disease. To establish normal electrocardiographic parameters were used Garson's criteria. The authors noted that all DMD patients showed sinus rhythm at ECG recording, but at 78.6% were objectified anomalies represented by: short PR interval in 18.3% of cases, sinus tachycardia in 2.2%, abnormal R wave in V1 in 29.7%, abnormal Q wave in V6 in 21.3%, changes in ventricular re-polarization in 54.9%, right bundle branch block in 7.6%, prolonged QT interval in 35.8%, large QRS complex in 23.6%, typical changes (ample R wave in V1 and deep Q wave in V6) in 6.8% of cases.

Also, Takani (2008) performed 136 ECG recordings from a group of 69 patients aged under 18 years, diagnosed with DMD, following potential cardiac electrical changes. The author observed that 91.3% of the studied children had one or more ECG abnormalities. He also noted that 84.8% of patients younger than 10 years had ECG changes, the most common being represented by the presence of a deep Q waves, and the typical appearance described in DMD represented by ample R wave in V1-V5 and deep Q wave was more common in adolescents.

Echocardiographic changes in children with Duchenne muscular dystrophy

In the past at young children under the age of 12 years diagnosed with DMD is appreciated that systolic cardiac function is normal, but recent studies have echocardiographic demonstrated the presence of subclinical cardiac dysfunction in this group of patients (Mertens, 2008). Thus echocardiographic is necessary at the comprehensive evaluation of pediatric age patients with DMD. In children with

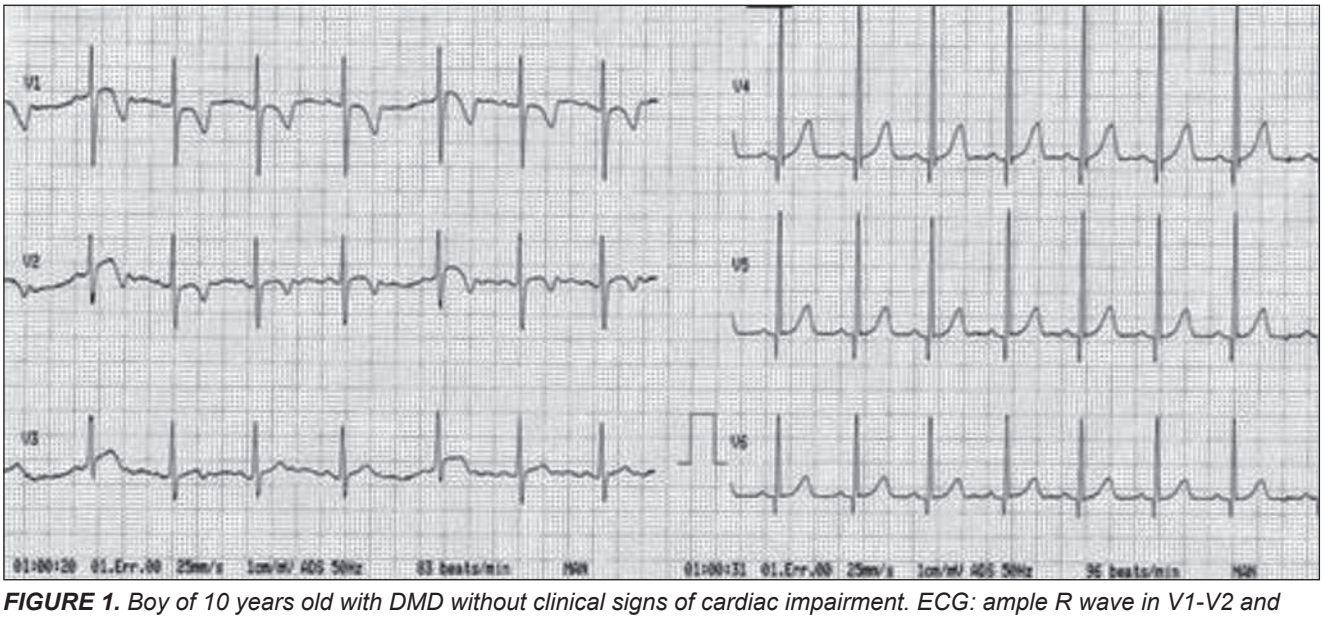

FIGURE 1. *Boy of 10 years old with DMD without clinical signs of cardiac impairment. ECG: ample R wave in V1-V2 and deep Q wave in V5-V6 (Collection of Pediatric Neurology Clinic)*

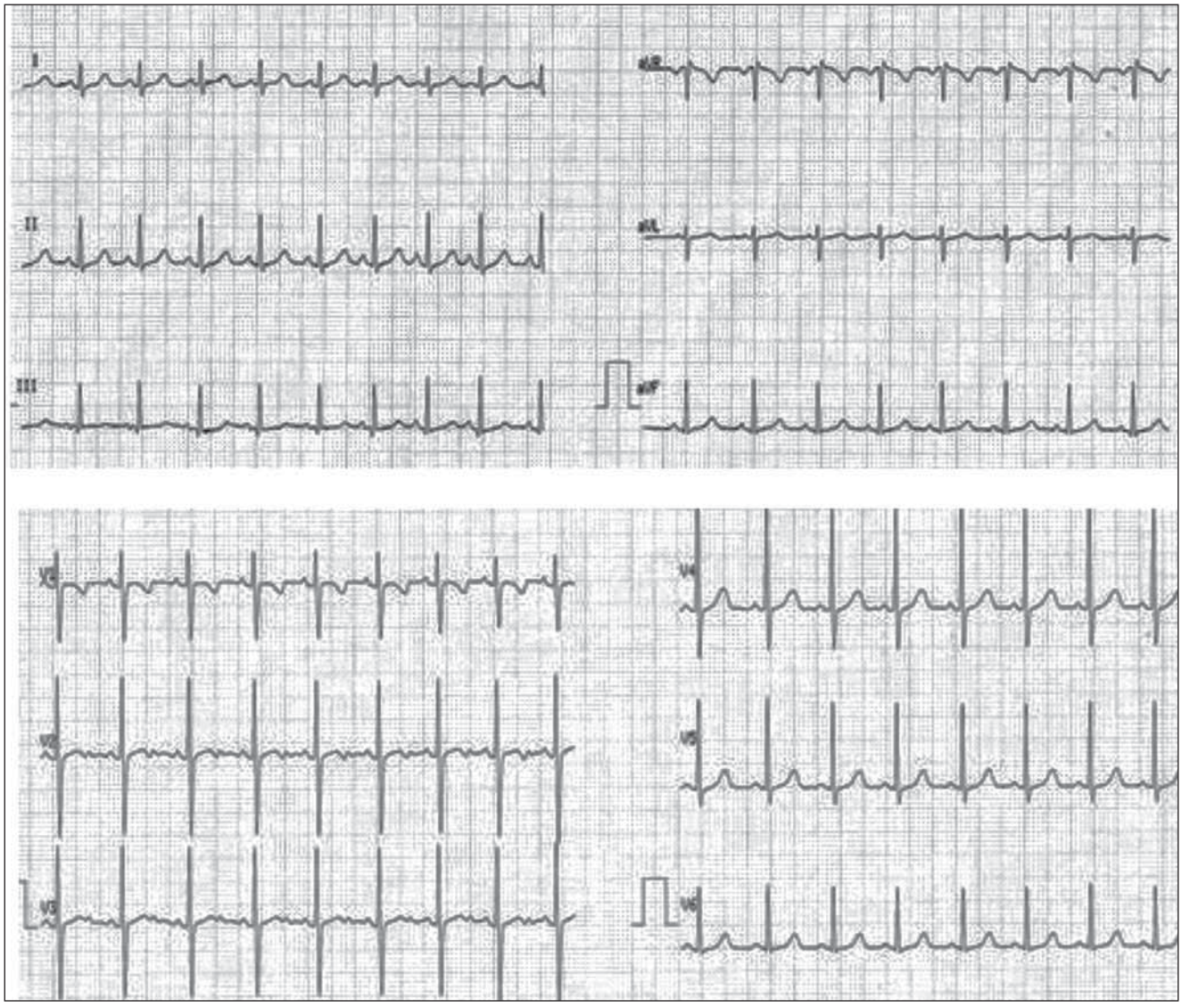

FIGURE 2. *Boy of 4 years old with DMD without clinical signs of cardiac impairment. ECG: QT = 0.35 sec (prolonged) (Collection of Pediatric Neurology Clinic)*

DMD where the echocardiographic standard examination is normal, myocardial performance index is a useful parameter in early detection of asymptomatic cardiac abnormalities (Shabanian, 2011).

Lee (2014) believes that in patients with DMD are structural and functional changes in the myocardium. The author echocardiographic explored (M-mode) 42 children with DMD and revealed atrophy in the left ventricular myocardium which was correlated with systolic function impairment and a low body mass index for age.

Gulati et al (2005) studied cardiac damage in a group of 30 children less than 6 years diagnosed with DMD with different motor impairment, 11 children having kept walking at the time of enrollment and 10% having clinical signs due to cardiac dysfunction. Approximately one third of patients were echocardiographic diagnosed with cardiomegaly, at 64.2% left ventricular ejection fraction was <55% and at 17.8% left ventricular ejection fraction was <50%.

In another study was echocardiographic evaluated 32 children with DMD aged 3-12 years, the authors concluded that patients with DMD who had normal global systolic function can present slowdowns of diastolic myocardial contraction speed in the anterior and lateral wall of the left ventricle and in the inferolateral wall of the left ventricle (Mertens, 2008).

Cardiac involvement at cardiovascular magnetic resonance in children with Duchenne muscular dystrophy

In recent years cardiovascular magnetic resonance (CMR) is increasingly being used for diagnosis and follow of the evolution of cardiac damage in patients with DMD. Cardiovascular magnetic resonance provides informations both on left ven-

tricular systolic function and myocardial tissue changes and occurrence of fibrosis (Florian, 2014). Cardiac lesions revealed at CMR are rarely observed before the age of 10 years (Bushby, 2010). It was also noted that the prevalence of myocardial fibrosis increases with age and can cause the decreases of the left ventricular ejection fraction (Hor, 2013). Verhaert (2011) believes that in patients with DMD the cardiomyopathy is caused by subepicardial fibrosis of the inferolateral wall, similar with the pattern observed in patients with viral myocarditis. Wansapura (2010) demonstrated at the CMR T2 signal changes, tissue edema and decreased left ventricular ejection fraction representative for micro fibrosis.

Walcher (2011) imaging cardiovascular studied a small group of 7 boys with DMD and concluded that the lesions of fibrosis are present before clinical onset of ventricular dysfunction. In turn, Bilchick (2011) assessed the prevalence and distribution of fibrotic lesions in the myocardial dysfunctional segments, on a group of 16 patients with DMD, noting that the prevalence of fibrosis at the inferior, inferolateral and anterolateral cardiac level was eight times higher than inferoseptal, anteroseptal and anterior segments.

In a study from 2013, which followed 314 patients with DMD, aged 6-28 years, Hor et al showed lesions of cardiac fibrosis in 30% of patients to whom the left ventricular ejection fraction was ≥ 55% and in 84% of those in whom left ventricular ejection fraction was <55%, noting that the prevalence of cardiac damage at CMR examination increases with age being 17% in children <10 years, 34% in those aged between 10-15 years of age and 59% in patients > 15 years.

CONCLUSIONS

- Cardiac manifestations are often found in children with Duchenne muscular dystrophy, representing, after respiratory failure, the most common cause of death.
- In children with Duchenne muscular dystrophy laboratory investigations should include ECG, Holter monitoring, cardiac ultrasound and cardiovascular magnetic resonance.
- Increased sensitivity of cardiovascular magnetic resonance in the early detection of abnormalities or minor changes in myocardial allows to better establish the natural progression of heart damage in Duchenne muscular dystrophy and allows the development of new therapeutic approaches for these patients.

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