J Neurol (2009) 256:283–284
DOI 10.1007/s00415-009-0055-7

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Cardiac magnetic resonance imaging and management of dilated cardiomyopathy in a Duchenne muscular dystrophy manifesting carrier

Received: 29 February 2008
Received in revised form: 7 June 2008
Accepted: 7 July 2008
Published online: 27 February 2009

Sirs: Duchenne muscular dystrophy (DMD) is an X-linked recessive disorder caused by a deficiency of dystrophin in skeletal and cardiac muscles. Most DMD boys initially present delayed motor milestones, elevated serum creatine kinase (CK), respiratory impairment and 25 % of those surviving the age of 15 present dilated cardiomyopathy and arrhythmias [3, 4, 8, 10]. Echocardiography describes left ventricular dysfunction, but cardiac magnetic resonance (CMR) can detect the earliest signs of cardiomyopathy: occult regional cardiac asynergy; tissue degeneration; fibrosis [1, 9, 12]. Standard therapy for heart failure is effective in DMD cardiomyopathy [7, 10].

Female carriers show a mosaic pattern of dystrophin-positive and dystrophin-negative muscular fibres. About 50 % of patients present skeletal muscular symptoms and 18 % present dilated cardiomyopathy, because of a "skewed X-inactivation", with most cells having an active faulty X-chromosome [5, 6].

A 27-year old woman was referred to our hospital in 2005 because of fatigue, effort dyspnoea (NYHA class IIb), episodes of palpitations and near syncope. Two brothers with a typical history of DMD without heart involvement died in their teens due to respiratory failure. Her asymptomatic 6-year old daughter had a mild increase of CK (640 U/L). DNA analysis revealed dystrophin gene deletion of exons 3–17. Electromyography showed small duration motor unit potentials and reduced amplitude interference pattern during voluntary contraction. In 2003, she had already been diagnosed with a dilated cardiomyopathy, with an echocardiographic ejection fraction (EF) of 40 %, treated discontinuously with carvedilol 6.25 mg b.i.d. She was a smoker (5 cigarettes/d) and showed only calf pseudohypertrophy.

She had high plasmatic concentrations of CK (1745 U/L, n.v. 22–269), normal levels of cardiac troponin I (0.02 ng/mL, n.v. < 0.5 ng/mL), plasma renin activity (1 ng/mL/h, n.v. 0.2–2.8) and noradrenaline (306 pg/mL, n.v. < 500), and borderline concentrations of aldosterone (157 pg/mL, n.v. 20–180) and NT-proBNP (142 ng/L, n.v. < 157). Her 24-hour ECG showed sinus rhythm, incomplete right bundle branch block, a paroxysmal supraventricular tachycardia and Lown class IV ventricular arrhythmias. Echocardiography confirmed the dilated cardiomyopathy (EF 33 %). CMR showed left ventricular dilation (end-diastolic volume, EDV, 126 ml/m^2, n.v. 56–99), diffuse hypokinesia (EF 35 %), with preserved left ventricular mass (62 g/m^2, n.v. 37–67) and right ventricular function (EDV 91 ml/m^2, n.v. 48–103; EF 50 %) (Fig. 1 a). Moreover CMR showed small areas of gadolinium delayed enhancement, suggestive of intramyocardial fibrosis, in the lateral wall and in septal junctions (Fig. 1 b). An intracardiac electrophysiological study revealed an inducible slow-fast reciprocating tachycardia, treated by radio-frequency catheter ablation of the slow pathway, without sustained ventricular tachycardias. Carvedilol was uptitrated to 25 mg b.i.d; ramipril 2.5 mg/d and spironolactone 25 mg/d were introduced. The patient then started a regular physical aerobic training program, 30–40 min cycloergometer sessions three times a week, at a work level under 60 % of VO_{2max}.

After discharge she reported a stable clinical status (NYHA class IIa). Two years later she still had increased CK (2051 U/L) and NT-proBNP (238 ng/L), but slightly reduced plasmatic aldosterone (92 pg/mL), noradrenaline (162 pg/mL) and renin activity (0.81 ng/mL/h). Her 24-hour ECG documented reduced ventricular arrhythmias without significant supraventricular arrhythmias. CMR showed a stable left ventricu-

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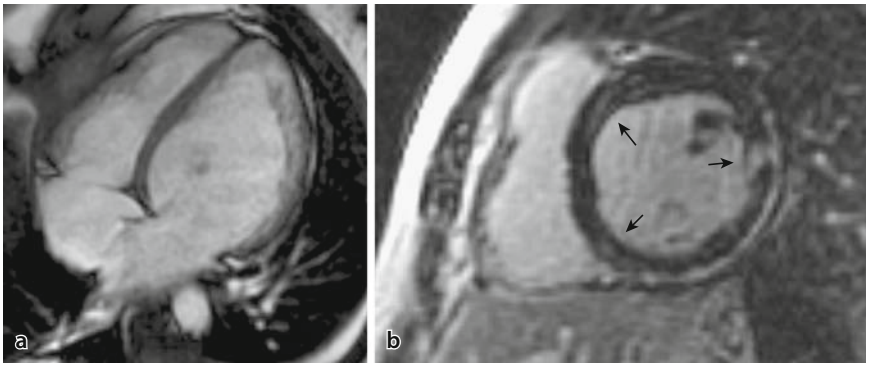

Fig. 1 **a** CMR (1.5 T, Signa CV/i GE Healthcare, Milwaukee, Wisconsin) steady-state free precession (SSFP) 4-chamber image of the heart, showing a mildly enlarged left ventricle with normal wall thickness. **b** CMR post-contrast T1-weighted inversion-recovery GRE short-axis view of the heart, showing areas of intramyocardial fibrosis (arrows) in the basal lateral wall and anteroseptal and inferoseptal junctions

lar dilation (EDV, 128 ml/m^2), an improved systolic dysfunction (EF 42 %), normal ventricular mass (67 g/m^2) and right ventricular function (EDV 101 ml/m^2; EF 51 %); the fibrotic areas were unchanged.

This case report highlights the likely occurrence of cardiomyopathy and arrhythmias in DMD carriers despite the minimal involvement of skeletal muscles, probably related to the different mechanisms of dystrophin gene regulation in cardiac and skeletal muscles [2]. The absence of significant neurohormonal activation agrees with previous observations [11]. CMR allowed a precise quantification of cardiac morphology and function; gadolinium revealed "spotty" intramyocardial fibrosis, probably deriving either from the chimerical distribution of "healthy" and "diseased" cardiomyocytes or from the heterogeneous distribution of myocardial wall stress damage.

Moreover, our case shows the beneficial effect of an optimized medical therapy on symptoms and cardiac function, compared to the natural progression of the disease.

Conflict of interest The authors declare no conflict of interest.

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