CASE REPORT

Successful treatment of end-stage hypertrophic cardiomyopathy with biventricular cardiac pacing

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Submitted 16 December 2003, and accepted after revision 3 December 2004

Abstract
The beneficial use of biventricular pacing is reported in a patient with end-stage hypertrophic cardiomyopathy, intraventricular conduction delay and echocardiographic evidence of intraventricular dyssynchrony. Marked improvement in clinical status, left ventricular ejection fraction and peak VO2 were observed. As far as we know, this is the first report of a beneficial effect of a biventricular device in this subset of patients, and may be worth further investigation.

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Introduction
A small subgroup of patients — less than 5% — with non-obstructive hypertrophic cardiomyopathy (HCM) develops systolic ventricular dysfunction and severe heart failure as a result of left ventricular wall thinning and chamber enlargement [1,2]. These patients are usually treated with afterload-reducing drugs such as ACE inhibitors, digitalis, diuretics, and beta-blockers, but many of them become candidates for heart transplantation [3]. We describe a case of a young patient with end-stage HCM successfully treated with biventricular pacing.

Case report
A 43-year-old male with a 15-year history of HCM was admitted in November 2002 because of progressive dyspnoea on mild effort. In 1988 diagnosis of non-obstructive HCM was made during routine echocardiographic screening prompted by several cases of HCM and sudden premature cardiac deaths being recorded in the patient’s family.

Echocardiographic examination performed in 1988 showed mild septal asymmetrical hypertrophy (15 mm), no midventricular obstruction, mild mitral regurgitation and preserved left ventricular systolic function ejection fraction (LVEF) 0.65.
The patient did well without medical therapy till 1995, when LVEF began to worsen. Despite treatment with enalapril progressive worsening of left ventricular systolic function was observed (LVEF 0.52 in 1995, 0.47 in 1997, and 0.37 in 2001), with mild left ventricular dilatation (end-diastolic diameter 65 mm in 2001) and moderate mitral regurgitation.

In 2001 the patient was in NYHA class II and in Weber class B on the cardiopulmonary testing (peak VO$_2$ 21 ml/kg/min, modified Balke protocol). Carvedilol was introduced in doses up to 12.5 mg per day. During the following year the patient’s symptoms, mainly dyspnoea and asthenia, continued to worsen; finally he was admitted because of dyspnoea NYHA III.

Resting ECG showed sinus rhythm with first degree atrio-ventricular block (PR 240 ms) and a very wide QRS complex, up to 230 ms. QRS morphology was bizarre. It appeared to be composed of two different deflections, as if after rapid septal activation impulse propagation in the left ventricle was very slow (Fig. 1).

Echocardiography showed severe left ventricular systolic dysfunction (LVEF 0.29, end-diastolic LV diameter 71 mm), moderate mitral regurgitation, and the presence of ventricular dyssynchrony, with increased mechanical interventricular delay (85 ms) and left ventricular segmental postsystolic contraction. Cardiopulmonary testing confirmed the severity of the haemodynamic status, with peak VO$_2$ 14.4 ml/kg/min (Weber class C). Coronary angiography excluded coronary artery disease.

Because of progressive worsening of clinical status despite optimal medical treatment (enalapril, carvedilol, diuretics, and spironolactone), the patient was to be scheduled for heart transplantation. Echocardiographic data and the QRS morphology raised the possibility of implantation of a biventricular device. After obtaining the patient’s informed consent a biventricular ICD (Renewal 2, Guidant) was implanted. The left ventricular lead (Easytrack, Guidant) was positioned in left lateral medio-basal cardiac vein (Fig. 2). Left ventricular sensing was 15 mV, slew rate > 4 V/s, pacing threshold 0.5 V × 0.5 ms, pacing impedance

Figure 1 Pre-implant ECG: unpaced, PR 240 ms, QRS duration 230 ms.
1373 ohm. Post-implant duration of paced QRS was 160 ms (Fig. 3). The decision to implant an ICD was made because of the malignant family history of premature sudden deaths and as a bridge to cardiac transplantation [4].

The patient was discharged on medical therapy (carvedilol 12.5 mg daily, ramipril 10 mg daily, spironolactone 25 mg daily) after a week.

One month later the patient reported an impressive improvement in subjective clinical status, total
disappearance of asthenia and dyspnoea NYHA II. Echocardiography showed an initial improvement in left ventricular systolic function (LVEF 0.36, end-diastolic LV diameter 65 mm), mild mitral regurgitation, absence of ventricular dyssynchrony (mechanical interventricular delay < 40 ms).

After 12 months the clinical improvement persists, with no dyspnoea on effort, Weber B on cardiopulmonary testing (peak VO2 21 ml/kg/min), echocardiographic LVEF 0.42. Medical therapy has not been changed.

Up to now, no ventricular arrhythmias have been detected by the device.

Discussion

Clinical trials have demonstrated significant benefits of cardiac resynchronization therapy on functional class, exercise tolerance, quality of life, hospitalizations and mortality in patients with advanced heart failure and dilated or ischaemic cardiomyopathy [7,8]. The ACC/AHA/NASPE 2002 guidelines have designated DDD pacing with right ventricular apical stimulation for severely symptomatic and medically refractory HCM patients with LV outflow obstruction as a class IIB indication [9], and a single case of beneficial use of biventricular pacing in a patient with severe obstructive HCM has been reported [10].

As far as we know, this is the first case of end-stage HCM successfully treated with biventricular pacing. Only a subset of patients with HCM (less than 5% of the total) shows a progressive deterioration in left ventricular systolic function with dilatation and wall thinning, usually after a long history of the disease. Drug treatment of end-stage HCM involves conversion to anti-heart failure drugs, such as ACE inhibitors, diuretics, digitalis and beta-blockers. In contrast to dilated cardiomyopathy, however, beta-blocking drugs seem not to be able to prevent progressive left ventricular dysfunction. This subgroup of patients, therefore, may become candidates for heart transplantation [1,2].

The progressive worsening of systolic function is thought to be due to fibrous transformation of intercellular connective tissue in the setting of myocardial fibre disarray or to a progressive loss of contractile apparatus [5,6]. Even if histological data are lacking, it is possible that a major amount of fibrosis of connective tissue could worsen the dyssynchrony of contraction caused by myocardial fibre disarray, thereby altering the geometry of the left ventricle, increasing wall stress, and eventually leading to wall thinning, increased end-systolic volume, and a reduction in ejection fraction. The clinical improvement in our patient, together with echocardiographic signs of reverse left ventricular remodelling, suggests that reduced LVEF in end-stage HCM can be due, at least in some cases, to ventricular dyssynchrony caused by intercellular fibrosis and not to the progressive loss of sarcomeres due to small vessel disease or atherosclerotic artery disease.

Conclusions

Biventricular pacing can, at least in some patients with end-stage HCM, induce reverse remodelling in the left ventricle, with improvement in LVEF and in haemodynamic status. Better systolic performance can be due to increased efficiency of contraction after biventricular pacing, which reduces intraventricular dyssynchrony. If this holds true, biventricular pacing could become a useful tool in this subset of patients.

References