Non Surgical Septal Reduction Therapy for Hypertrophic Obstructive Cardiomyopathy

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INTRODUCTION

Hypertrophic obstructive cardiomyopathy (HOCM) is a genetic disorder associated with significant morbidity and mortality. Patients with this illness are prone to sudden death, angina, syncope, and heart failure. Symptomatic patients with HOCM are usually medically treated; in the few patients with persistent symptoms, surgical myomectomy offers satisfactory control.[1,2] The role of DDD pacing in effort to reduce left ventricular outflow tract (LVOT) gradient is still controversial.[3,4] Recently, non-surgical septal reduction therapy (NSRT) has gained popularity as an alternative to surgery, because the procedure is much simpler, safe and effective for relief of symptoms of LVOT obstruction.[5-7]

This paper will report a case of HOCM successfully treated with NSRT.

CASE

A 56 years old gentleman came with symptoms of exertional chest pain which became aggravated since one year. He did not have complaints of dyspnea nor syncope. He had a history of dyslipidemia, but hypertension, diabetes mellitus, or cigarette smoking was denied. On physical examination, he was found to have systolic ejection murmur in the left parasternal area and holosystolic murmur in the apex. His ECG showed left venticular hypertrophy, and downsloping ST depressions with deep negative T waves in leads I, aVL, and V5-6. Chest film showed mild cardiomegaly. Echocardiography was compatible with HOCM with interventricular septal thickness of 22 mm, systolic anterior movement of the mitral valve, and mitral regurgitation. Flow in the LVOT was turbulent and the peak LVOT pressure gradient was 95 mmHg. Cardiac catheterization subsequently performed and this documented LV pressure of 288/22 mmHg, aortic pressure 143/108/120 mmHg, (LVOT gradient 145 mmHg at rest). Global LV contractility was normal with ejection fraction 81%. There was grade III mitral regurgitation. All coronary arteries were normal.

During the NSRT procedure, the left ventricular pressure gradient was continuously recorded by placing one pig-tail catheter in the left ventricular cavity and another catheter in the aorta. Temporary transvenous pacemaker was inserted to avoid the potential problem of transient bradyarrhythmias or AV block. Catheterization of the target vessel (the most important proximal septal perforator) was performed by standard angioplasty techniques. A 2.0/20 mm over-the-wire balloon was chosen and introduced to the target vessel. The balloon selected was slightly bigger than the target vessel. The balloon was inflated taking care to place the proximal end of the balloon exactly at the ostium of the target vessel to avoid injury or partial flow obstruction in the left anterior desending coronary artery. While the balloon was in full expansion, the guide wire was pulled out. Full strength contrast medium was then injected to the left coronary ostium via the guiding catheter. Absence of contrast filling to the target vessel confirmed that the balloon was completely occlusive to the target vessel. Three-to-5 cc half strength contrast media was then injected manually through the lumen of the inflated balloon. The target territory was delineated by the contrast visualized branches of the target vessel. The tactile sensation of the increasing resistance during injection gave an idea of the approximate amount of alcohol to be injected for septal reduction therapy. Particular attention was also given to the absence of retrograde filling to the left anterior descending coronary artery as any spill over would invariably sclerose this important parent vessel should this happen during alcohol injection. Subsequently, 3-5 cc of desiccated alcohol was injected very slowly through the

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balloon lumen to the target vessel. Meticulous care was taken not to use forceful injection to avoid pushing back the balloon and spilling over of the alcohol to the left anterior descending coronary artery. Injection was stopped when significant resistance was felt. The baseline LVOT gradient 80 mmHg, 108 mmHg during nitrate challenge and 198 mmHg after postextrasystolic provocation (induced by catheter manipulation). LVOT gradient significantly decreased to 21 mmHg during balloon inflation. At the end of procedure it was only 6 mmHg at rest, 12 mmHg during nitrate challenge, 69 mmHg after postextrasystolic potentiation. The characteristic "dome and dart" shape of the aortic pressure in HOCM disappeared after NSRT. Repeat contrast injection to the left coronary artery confirmed the complete amputation of the target vessel at its proximal segment and intact left anterior descending coronary artery. There was no complication. The patient did not show significant complaint of chest pain. There was no ECG changes during or after the procedure. CK and CK-MB levels were 22 u/l (normal: < 80 U/l) and 4 U/l)normal: < 4 U/l) before NSRT, and these values increased to 289 U/l and 30 U/l after NSRT. On echocardiography, after NSRT, the interventricular septal motion became hypokinetic, mitral regurgitation was less severe, LVOT turbulence decreased and LVOT gradient declined to 59 mmHg. The patient was discharged on the day after the procedure. On clinical follow-up period of 12 months, he was symptomatically improved.

DISCUSSION

Hypertrophic cardiomyopathy is a genetic disorder with an autosomal-dominant inheritance.[8,9] In most patients, the hypertrophy develops initially in the septum and extends to the free walls, often giving a picture of concentric hypertrophy. In approximately 25% of patients asymmetrical septal hypertrophy leads to a variable pressure gradient between the apical left ventricular cavity and the left ventricular outflow tract (LVOT). LVOT obstruction (or hypertrophic obstructive cardiomyopathy [HOCM]) with a consecutive increase of left ventricular pressure fuels to a vicious circle of further hypertrophy and increased LVOT obstruction. In most patients with LVOT obstruction, the hypertrophy is most pronounced in the high intraventricular septum compared with the rest of the left ventricle. Patients with significant LVOT obstruction have systolic anterior motion of the mitral valve associated with the LVOT obstruction, which leads to mitral regurgitation.[2,8,9] LVOT obstruction may be present at rest or can be induced with the Valsalva maneuver or with dobutamine, isoproterenol infusion, or amylnitrate inhalation. In addition to LVOT obstruction, disabling symptoms may be associated with impaired left ventricular diastolic and systolic dysfunction, myocardial ischemia, and arrhythmias.[7-9]

Clinical manifestations of HOCM may be present in early childhood or may develop much later in life. The most common clinical manifestation is dyspnea, followed by chest pain, with or without syncope or presyncope. Unfortunately, all too often, the first symptom is sudden cardiac death without any warning. HOCM is the most common cause of sudden death in the young.[10] Most HOCM patients have two murmurs: midsystolic ejection murmur from LVOT obstruction and holosystolic murmur due to mitral regurgitation. The mitral murmur varies greatly with a number of interventions, including those designed to change the cavity size (eg. squatting, Valsalva maneuver, and amylnitrate inhalation) and contractility (eg. dobutamine, isoproterenol, and endogenous cathecholamines)[11] The ECG is often abnormal, showing left ventricular hypertrophy and/or nonspecific ST changes with Q waves in II, III, and aVF. The diagnosis is confirmed by echocardiography showing hypertrophy of the septum and ventricular wall, being more pronounced in the septum, LVOT obstruction, systolic anterior motion on the mitral valve with mitral regurgitation.[11]

Numerous treatment options have been suggested for HOCM with the primary aim to relieve LVOT obstruction.

Drugs that lower left ventricular contractility (β-blockers, verapamil, and disopyramide) or increase peripheral vascular resistance (methoxamine), or both are considered beneficial. β-blockers are usually considered as the basic therapy for patients with HOCM. In patients who do not tolerate β-blockers, calcium antagonists with negative inotrophic effect (eg. verapamil) is a good alternative. Disopyramid is also sometimes used, because it has a negative inotrophic effect, it alters calcium kinetics and produces a peripheral vasoconstrictor effect. Similar results have been reported with cibenzoline, a class 1a antiarrhythmic drug. Most patients experience improvement in chest pain and dyspnea after the introduction of negative inotrophic substances. Whether the drugs have long term impact in the natural history of the disease remains unknown.[1,2,7-9]

Another avenue of treatment is surgical myomectomy. The procedure consists of excising of a portion of the thickened septum to reduce the intraventricular gradient. It may be combined with surgery of the mitral valve. The operation normally results in a permanent sig-

Figure 1. A. Left coronary angiogram. Target vessel is the proximal and biggest septal perforator artery (closed arrow). Open arrow indicates the left anterior descending coronary artery. B. Disappearance of the target vessel after alcohol injection.

nificant reduction or abolition of intramyocardial gradients and reduction in mitral incompetence. There is also long-term improvement in symptoms and exercise capacity in most patients. However, the procedure carries a significant mortality rate, being reported to be <2% to 5%.[1,2]

Dual-chamber DDD pacemaker insertion is based on the observation that excitation of the septum of the left ventricle contracts it away from the opposing wall, which may reduce the LVOT gradient. Although a European study suggested benefit of pacing therapy with regard to symptoms, this finding is not substantiated by several recent studies in the United States.[3,4]

The beneficial effects of myomectomy led to the concept pf NSRT. The first clinical experience in 1994 was based on earlier observation that temporary suppression of myocardial blood supply to the upper intraventricular septum resulted in an immediate reduction in the LVOT gradient in a patient with HOCM. Subsequently in the same year 3 patients underwent NSRT. Three-to-5 cc of desiccated alcohol was infused distal to the angioplasty balloon into the first septal perforator of the left anterior descending artery to ablate the upper septum. None of these patients had significant morbidity and all 3 are still alive.[5] Because the procedure is relatively easy and not costly, morbidity is relatively minor, whereas the success rate is excellent; it was readily adopted by many investigators. A reduction of LVOT at the time of procedure is desirable, but is not mandatory for long-term success. Clinical evaluation from several centers confirms that NSRT is a safe and effective procedure for the relief of symptoms and LVOT obstruction long-term.[6,7]

The current criteria for NSRT are:[7]

1. Symptomatic patients who have contraindications, or are resistant to drug treatment, or need to reduce their medical therapy
2. LVOT gradient ≥ 30 mmHg (at rest), or ≥ 60 mmHg at provocation (eg. dobutamine or isoproterenol infusion, Valsalva maneuver, or postextrasystolic potentiation)
3. Septal thickness > 18 mm
4. Systolic anterior motion of the mitral valve is observed on echocardiography.

By and large complications are rare and mostly benign. Potential complications included: transient chest pain during alcohol injection (1-2 minutes), benign arrhythmias (major arrhythmias such as ventricular tachycardia and/or fibrillation and transient or permanent AV block are rare). Other serious complications such as septal perforation (unlikely if septal thickness is > 18 mm), free wall perforation, papillary muscle infarction and tamponade are extremely rare. The reported hospital mortality varies between 0 and 4%; in the largest series to date (n=290) it was only 1%.[5-9]

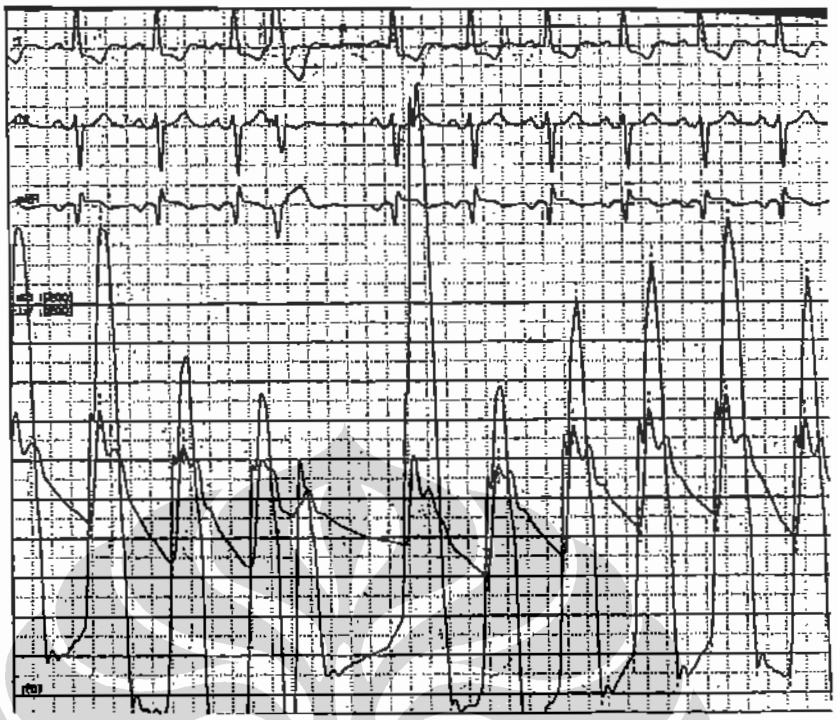

Figure 2. Pressure tracings at baseline. LV pressure 219/11 mmHg, aortic pressure 139/80/103 mmHg, LVOT gradient 80 mmHg. After postextrasystolic potentiation, LV pressure 320/64 mmHg, aortic pressure 122/78/93 mmHg, LVOT gradient 198 mmHg. Note the characteristic "dome and dart" shape of the aortic pressure.

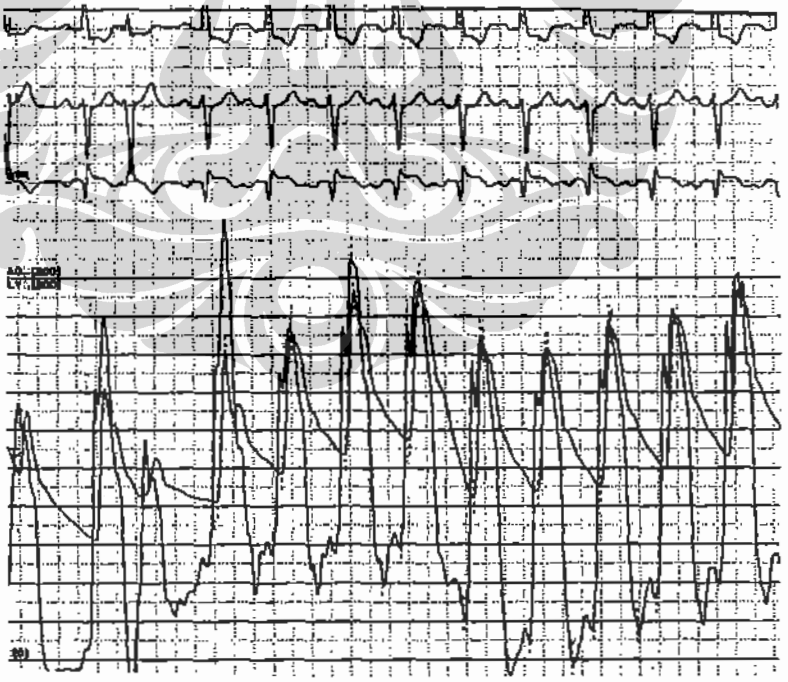

Figure 3. Pressure tracings at baseline. LV pressure 177/17 mmHg, aortic pressure 171/91/126 mmHg, LVOT gradient 6 mmHg. After postextrasystolic potentiation, LV pressure 230/49 mmHg, aortic pressure 161/62/95 mmHg, LVOT gradient 69 mmHg. Note the disappearance of the characteristic "dome and dart" shape of the aortic pressure; it is only apparent in the postextrasystolic aortic pressure curve.

CONCLUSION

NSRT is a safe, and effective procedure for eliminating or significantly reducing LVOT gradient and symptom relief in patients with HOCM.

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