

PERCUTANEOUS TRANSLUMINAL SEPTAL ABLATION - MODERN AND EFFICIENT THERAPEUTIC PROCEDURE IN SEVERE CASES OF OBSTRUCTIVE HYPERTROPHIC CARDIOMYOPATHY

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REZUMAT

În ultimii ani s-au înregistrat progrese în ceea ce privește rezolvarea pe cale invazivă a unor afecțiuni cardiace, printre acestea numărându-se și ablația septală transluminală percutană, procedură modernă și eficientă de tratament a cazurilor severe de cardiomiopatie hipertrofică obstructivă. Autorii acestui articol prezintă rezolvarea unui astfel de caz în cadrul Clinicii de Cardiologie a Institutului de Boli Cardiovasculare Timișoara.

Cuvinte cheie: cardiomiopatie hipertrofică obstructivă, gradient, ablație

ABSTRACT

In the last years there has been a real progress in resolving through invasive procedures different heart diseases, one of them being percutaneous transluminal septal ablation, a modern and efficient procedure for the treatment of severe cases of obstructive hypertrophic cardiomyopathy. The authors of this article describe such a case, resolved in the Clinic of Cardiology of the Institute of Cardiovascular Medicine Timisoara.

Key Words: obstructive hypertrophic cardiomyopathy, gradient, ablation

INTRODUCTION

Hypertrophic cardiomyopathy (HCM) is a relatively common familial cardiac disease with a broad clinical spectrum, for which the risk of premature cardiovascular death and incapacitating symptoms in young patients (including trained athletes), but not only, has been repeatedly emphasized.¹⁻⁴ HCM is a complex and relatively common genetic cardiac disorder (about 1:500 in the general adult population), that affects men and women equally and occurs in many races and countries.⁴

HCMs are myocardial diseases without an obvious cause, genetically, clinically, morphologically,

functionally heterogeneous, variable in their evolution, from asymptomatic forms to heart failure, arrhythmias and sudden death - the annual death toll averages around 1.2%, of which half represents sudden deaths.^{5,6}

The distinctive sign of HCM is the unexplained left ventricular hypertrophy (e.g., aortic stenosis or systemic hypertension), demonstrated echocardiographically or frequently in necropsy (after death). Because of its heterogeneous clinical course and expression, HCM represents a management dilemma to cardiologists and other practitioners. Furthermore, with the recent treatment strategies, targeting different subgroups of patients, many questions arise.⁴ Hence, the difficulty of identifying as early as possible, risks patients in order to prevent sudden death.

It is of clinical importance to distinguish between the obstructive and nonobstructive forms of HCM, based on the presence or absence of a left ventricle (LV) outflow gradient under resting and/or provokable conditions. Outflow gradients are responsible for a loud apical systolic ejection murmur associated with a

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Received for publication: Oct. 14, 2005. Revised: Dec. 9, 2005.

constellation of other clinical signs, hypertrophy of the basal portion of ventricular septum and small outflow tract, enlarged and elongated mitral valve. Obstruction may be subaortic or midcavity in location. Subaortic obstruction is caused by systolic anterior motion (SAM) of the mitral valve leaflets and mid-systolic contact with the ventricular septum. Obstruction in HCM is characteristically dynamic: the magnitude (or even the presence) of an outflow gradient may be spontaneously labile and vary with a number of factors (small amount of alcohol, heavy meal, etc.).⁴

CASE REPORT

We want to report the case of a young man, C.B., 27 years old, from rural environment, admitted in our Clinic in November 2002 with the following complaints: dyspnea at progressively smaller efforts, palpitations (that occurred 3-4 months before), thoracic discomfort at stress and medium effort, a minor syncope episode and a confirmed left parasternal systolic murmur, caught for the first time in a medical exam by the family doctor. Family history revealed that his father died of unspecified cause at the age of 56. The patient didn't show pathological personal history. Working and living environment were normal; ex-smoker (~10 years), 1 package/day, occasional alcohol and coffee consumer.

Clinical examination: height = 182 cm, weight = 70 kg (BMI = 21.13 kg/m²); hypostenic constitution; normal pulmonary sounds on auscultation; regular cardiac rhythm, heart rate (HR) = 72 b/min., blood pressure (BP) = 125/80 mmHg; ejection systolic murmur of maximum intensity V/V₆ in left intercostal parasternal space III-IV, exposure on all cardiac area, with no other modifications.

Biological: pathological: cholesterol = 303 mg/dl; all other exams with normal values.

ECG: regular sinus rhythm, left deviation QRS axis, HR = 84/min., terminal forces of P wave in V₁, QS aspect in DIII, aVF, V₁-V₃, horizontal-ascending ST elevation of ~ 2-3 mm in V₁-V₃, high T waves, symmetrical in V₂-V₄, QT interval of 0.38s. Figure 1 shows ECG aspect in 12 derivations (pre-interventional).

Thoracic X-ray: no acute pleural or pulmonary lesions; cord with prolonged inferior left arch.

2D Echocardiographic transthoracic exam: IVS (interventricular septum) = 2-2.2 cm, high echogenicity; LV-PW (posterior wall) = 1.1 cm; movement in systole of the mitral valve with SAM (systolic anterior movement) present; apical 4 chambers: parietal movement with global hyperkinesia; quantitative Doppler exam: mitral

flow: E = 1.29 m/s, A = 0.57m/s, E/A > 1; mitral regurgitation II/III degree; aortic flow: V_{max} = 7 m/s in the ejection tract of the LV; P_{max} ~ 240 mmHg and P_{med} ~ 120 mmHg; aortic regurgitation I degree. Figure 2 shows LV long axis view and apical 4 chambers view and Figure 3 the quantitative Doppler LV/Ao gradient.

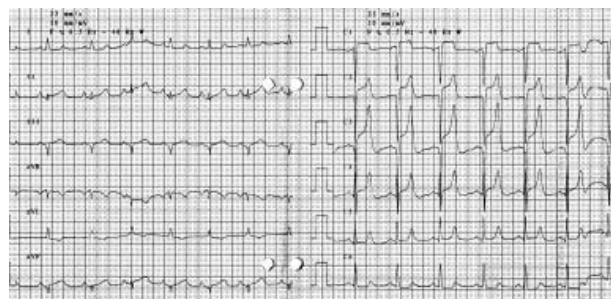


Figure 1. Pre-interventional ECG.



Figure 2. LV echocardiography - long parasternal axis and apical 4 chambers views.

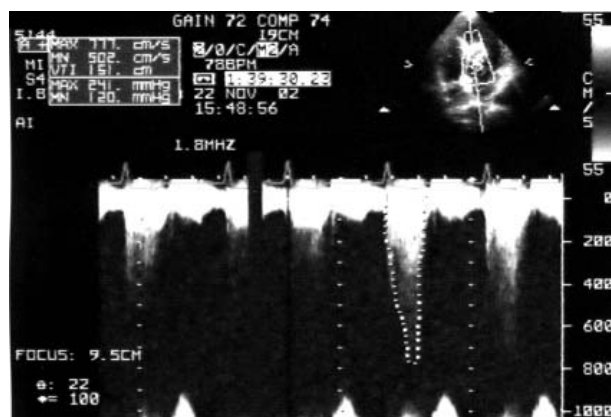


Figure 3. Echocardiography - LV/Ao gradient (quantitative Doppler).

Transesophageal echocardiography: severe SAM aspect; IVS = 1.8–2 cm; LV-PW = 1.3–1.4 cm; mitral regurgitation II/III degree; global LV hyperkinesia aspect; I degree tricuspidian regurgitation; without thrombus in LA (left atrium) or LA appendage; Pmax in TE–VS = 118 mmHg.

Continuous 24h ECG Holter: 2 episodes of unsustained VT (ventricular tachycardia), both in the early hours, a short SVPT (supraventricular paroxysmic tachycardia) episode, cardiac frequency variability in normal parameters. But, it should be kept in mind that Holter monitoring identifies only a small subset of patients at high risk and, therefore, the search for other risk factors is a must.⁷

Angio-coronaro-ventriculographic exam: Balanced coronary system, with no coronary lesions, except a muscular bridge on ADA (anterior descendente artery) in the middle section. The occlusion becomes visible in the ejection tract of the LV when injecting on the pig tail catheter in the LV. Maximum gradient LV/Ao = 120 mmHg, medium gradient of 90 mmHg. Mitral regurgitation of II/III degree.

Positive diagnosis: established at this moment of the evaluation:

1. *Obstructive hypertrophic cardiomyopathy with high LV/Ao gradient (severe form).*

2. *Secondary mitral regurgitation II/III degree.*

3. *Severe hypercholesterolemia.*

Differential diagnosis: for the systolic murmur: aortic stenosis, mitral valve prolapse ± mitral regurgitation; mitral regurgitation (including secondary ischemic mitral regurgitation); VSD; tricuspid regurgitation; pulmonary stenosis, but, all of these not being related to the pathology already affirmed. Septal eccentric hypertrophy differential diagnosis not determined.

Evolution - prognosis: Without a radical therapy annual mortality rate in obstructive HCM is ~ 4 % (indirectly dependant of the onset age of the disease; very high in individuals with frequent unsustained TV episodes, with syncopes, or resuscitated sudden death). Family history of sudden death, even angina, effort dyspnea in patients older than 45 offers often a dark prognosis.

The most frequent complication is sudden death; less frequently, the disease progresses with with initial heart failure.

A few years ago patients with high risk of sudden death were considered those with: age under 30 at the time of the diagnosis; family history of HCM with sudden death; genetic disorders; unsustained VT on 24h ECG Holter.⁸

The ACC/ESC Consensus Document on Hypertrophic Cardiomyopathy from 2003 describes the major risk factors for sudden death in HCM: cardiac arrest (ventricular fibrillation), spontaneous sustained ventricular tachycardia, family history of premature sudden death, unexplained syncope, LV thickness ≥ 30 mm, abnormal exercise blood pressure and non-sustained ventricular tachycardia (on Holter monitoring).⁴

Thus, dependent of the patient's age, there remains also the genetic advice. The patient is the father of a ~2 years old child in which echocardiographic examination was normal.

Treatment should be directed to the abnormal diastolic compliance of the LV and reduction of the major LV/Ao gradient; β -blockers, Ca^{++} blockers, alone or in association, represent the most used conservative treatment; both categories reduce myocardial contractility with cavity dilatation and diminishing the ejection tract (ET) obstruction, thus improving the LV diastolic function; moreover, reducing cardiac frequency, they prolong the LV filling duration, reducing ET obstruction; among Ca^{++} blockers the most chosen are those with weak vasodilation effect, with important depressing effect on myocardial contractility – e.g. Verapamil.

Infectious endocarditis prophylaxis is recommended.

Overdosed exercise is not recommended because of the high risk of sudden death linked to excessive effort.

Septal miotomy or miectomy is reserved for patients with severe, incapacitating symptoms, despite the prescribed and followed drug treatment. This procedure improves the symptoms, but it doesn't seem to reduce mortality.⁹

Selective septal embolization (percutaneous transluminal septal ablation by concentrated ethanol injection) may represent an alternative to septal miectomy, as it is obviously superior to it so far.^{9,10}

In some cases, a mitral valve replacement was made – the cases with severe mitral valve dysfunction, with decrease of the gradient in the ET of the LV.

The dual-chamber cardiac pacemaker implant was used in order to modify the LV depolarization sequence for some of the patients with obstruction in the ET of the LV, with the decrease of the obstruction severity and the improvement of the clinical picture. The long term effect, over the mortality too, needs further studying.

In our case, the drug treatment consisted of Verapamil 240 mg/day, Metoprolol 75 mg/day in a first phase, and later we added the invasive treatment called

percutaneous transluminal septal ablation, done for objective reasons, in January 2003 (after approximately 2 months from the first evaluation).

The therapeutic procedure consisted of the catheterism of the left main, with the mending of the first septal artery – proximal branch of the left anterior descending artery (ADA), artery that supplies the incriminated septal area (with maximum hypertrophy), viewed after injecting Levovist, through transthoracic echocardiography. Simultaneously, we placed the pig tail catheter in the LV. After that, we placed an ATW angioplasty guide in the first septal artery and a QTW 1.5-20 mm balloon behind the septal ostium, in its lumen, injecting two boluses of 2.5 ml 90% alcohol in the septal lumen isolated this way.

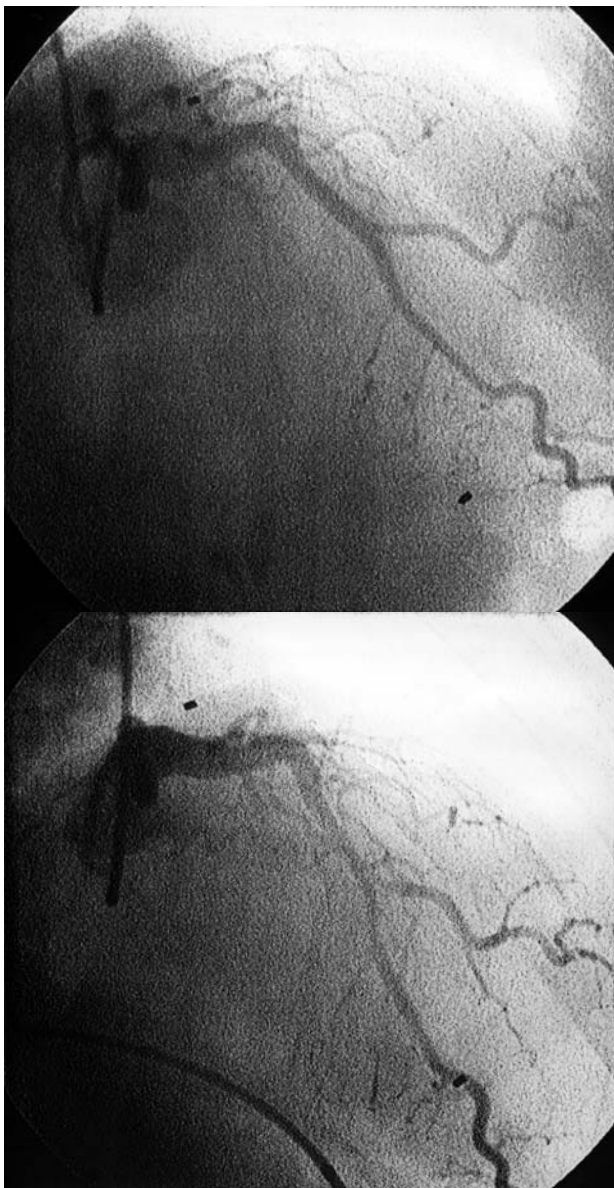


Figure 4. Angiographic aspect of the first septal before and after the embolization.

After a few minutes, with marked thoracic pain,

bradycardia, transitory total AV block (with VVI stimulated rhythm) and ventricular premature beats, without VT, with moderate decrease of blood pressure, we observed on the ECG a complete left bundle branch block, with normal AV conduction. After repeating the pig tail retraction from the LV into the aorta, we observed a difference between systolic LV/Ao gradient from 130 mmHg initially, to 23 mmHg at the end, with LV's TDP decrease from 48 mmHg initially to 19 mmHg immediately after the procedure, with base septal akinesia observed at transesophageal echocardiography, characteristic markers for the success of the procedure.



Figure 5. The aspect of the pre- (a) and post-interventional (b) retraction curve.

The whole procedure was made under the protection ensured by prophylactic placing a transitory stimulation catheter in RV.

Initial postprocedural evolution, under treatment with Metoprolol 150 mg/day, Diltiazem 180 mg/day, Aspirin 325 mg/day, Enoxaparin 80-140 mg/day, Cefazolin 3 g/day, Gentamicin 160 mg/day, was favorable, without the complications cited as possible during or after the percutaneous transluminal septal ablation:

- coronary dissection;
- trouble with intra V conductivity (especially complete BRD) and transitory or permanent complete A-V block (up to 50% of the treated patients), that

may necessitate procedural transitory stimulation (as we did in our case) or permanent pacemaker;¹¹

- ventricular arrhythmias: repetitive, sustained VT, requiring implantable defibrillator;

- unwanted myocardial infarction – at another level than the desired one, through alcohol embolization in ADA.

Six days after the procedure, the transitory stimulation catheter has been removed. The maximum peak of myocardial enzymes (CK, CK-MB) was of 844 U/l, respectively 130 U/l, 12 hours after the procedure.

The transthoracic echocardiography done after the procedure revealed a IVS of 2.2 cm with high echogenicity, LV-PW of 1.5 cm, SF = 31% and LV-EF = 60%, with a slight outline of SAM; LV-EF(planimetric) = 51%; basic septal akinesia, medium septal hipokinesia; I/II degree of mitral regurgitation; flux in ET of LV with Vmax = 2.6 m/s and Pmax = 27 mmHg, and Pmedim = 13 mmHg.

The patient checked out on the seventh day after the procedure, with the recommendation of monthly follow-up.

Late evolution was favorable; the ambulatory treatment has been maintained: Metoprolol 150 mg/day, Diltiazem 180 mg/day and Aspirin 100 mg/day.

At the clinic and echocardiographic check-ups, made after 1 and 3 months from the procedure, obviously positive changes have been noticed: absence of the pre-procedural symptoms, increase of the effort capacity, marked decrease of the systolic ejection murmur (gr. II/VI), complete LBBB persistence on the EKG (Fig. 6), and asymmetrical LVH echocardiography with a IVS of 1.7 cm, LV-PW of 1.25 cm, LV-EF (planimetric) of 60%, akinesia of the IVS basic segment, without ET-LV gradient (Vmax = 2 m/s, Pmax = 16 mmHg, Pmedium = 8 mmHg), as Figure 7 shows.



Figure 6. Post-interventional ECG with persisting LBBB.

Our patient's 38 years old sister, asymptomatic and without major pathological antecedents, M.B., has been clinically and echocardiographically evaluated.

The echocardiography revealed a 1.36/1.52 cm IVS with echodense appearance, slightly motley, a 0.9/1.1 cm LV-PW, a 63% LV-EF (Teicholtz), without other modifications.

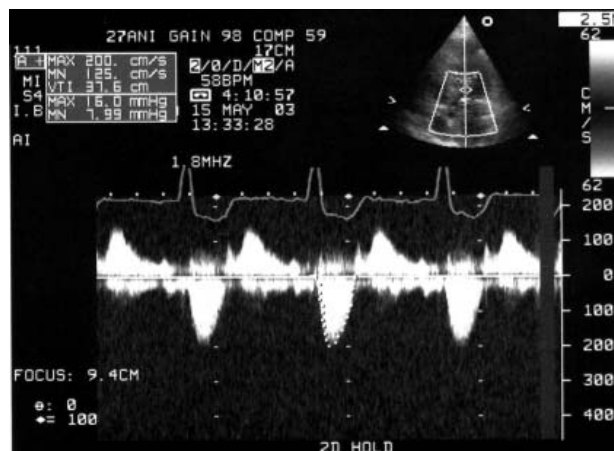


Figure 7. Post-procedural echocardiography - without LV/Ao gradient.

DISCUSSION

Why percutaneous transluminal septal ablation and not septal myectomy?

Surgery – the patients with HCM referred to surgical treatment have, usually, particularly marked outflow gradients (peak instantaneous usually ≥ 50 mmHg), as measured with continuous wave Doppler echocardiography.⁴ In addition, these patients have severe limiting symptoms (exertional dyspnea and chest pain, regarded as NYHA functional classes III or IV, refractory to maximum medical therapy).

Over the past four decades, based on the experience of a number of centers throughout the world, the ventricular septal myectomy operation (the Morrow procedure) has proven useful for the amelioration of outflow obstruction and for both, adults or children, with obstructive HCM and severe drug-refractory symptoms.⁴ But, the myectomy operation should be confined to experienced centers in this procedure.

In 1995 Sigwart described for the first time the effect of the occlusion with ethanol of a perforating artery on the pressure gradient from obstructive HCM. The procedure induced septal MI.¹¹ Septal ablation mimics the hemodynamic consequences of myectomy by reducing the basal septal thickness and excursion, producing akinetic or hypokinetic septal motion, enlarging the LV outflow tract and lessening the SAM of the mitral valve and mitral regurgitation.⁴

Table 1 presents the comparison between septal myectomy and percutaneous alcohol septal ablation.⁴

Table 1. Comparison of septal myectomy and percutaneous alcohol septal ablation.

Parameter	Myectomy	Ablation
Operative mortality	1-2%	1-2%
Gradient reduction (at rest)	< 10mmHg	< 25mmHg
Symptoms (subjective)	decreased	decreased
Symptoms (objective)	decreased	decreased
Effectiveness despite anatomic variability	usually	uncertain
Pacemaker (high grade A-V block)	1-2%	5-10%
Procedure frequency	x	15-20x
Sudden death risk (long-term)	very low	uncertain
Available follow-up	> 40 years	~ 6 years
Intramyocardial scar	absent	present

There are a lot of centers that have surgical experience and frequently perform septal myectomy. At present, some of them do ethanol ablation, but there is not enough expertise with both procedures by comparison.

In our case we have chosen the percutaneous alcohol septal ablation due to the patient characteristics and, of course, due to the correct angiographic identification of the perforating septal branch that had to be occluded, avoiding the occlusion of the septal perforating arteries that supply the myocardial areas that were not part of the pathogenic process: papillary muscles, the free wall of the left or right ventricle.

Of course, it must be added the relative ease with which ablation can be performed (compared to surgery), - but only by an experienced team! - with substantially less discomfort during a much shorter postoperative hospitalization and recovery period, in the absence of a sternotomy. It must be remembered and emphasized again that the septal ablation therapy relies on the fixed anatomic distribution and size of the septal perforator coronary arteries.

CONCLUSIONS

The case we presented comes to emphasize the value of this new therapeutic procedure, in high severity obstructive HCM cases, completely documented invasive and non-invasive. The lack of intra- and post-procedural difficulties, the favorable evolution of the LV diastolic function, of the obstructive gradient LV/Ao from ET, of the mitral regurgitation, and even the relative quick decrease of the IVS thickness, without myocardial complications (conduction or of the rhythm changes), infectious or cerebral and peripheral vascular complications, recommend, once more the use of this procedure for all cases that do not respond efficiently to drug therapy, and mostly in the cases with high morbid or lethal risks.

REFERENCES

1. Maron BJ, Casey SA, Hauser RG, et al. Clinical course of hypertrophic cardiomyopathy with survival to advanced age. *JACC* 2003;42(5):882-8.
2. Wigle ED, Rakowski H, Kimball BP, et al. Hypertrophic cardiomyopathy. Clinical spectrum and treatment. *Circulation* 1995;92:1680-92.
3. McKenna WJ, Deanfield JE. Hypertrophic cardiomyopathy: an important cause of sudden death. *Arch Dis Child* 1984;59:971-5.
4. ACC/ESC Expert Consensus Document on Hypertrophic Cardiomyopathy. *JACC* 2003; 42(9):1687-713.
5. Gherasim L. *Progrese in Cardiologie*, Bucuresti: Infomedica, 2002.
6. Braunwald E. *Heart Disease – A Textbook of Cardiovascular Medicine*, 6th Edition, WB Saunders, 2001.
7. Hess OM. Risk stratification in hypertrophic cardiomyopathy – fact or fiction? *JACC* 2003;42(5):880-1.
8. Moon JCC, McKenna WJ, McCrohon JA, et al. Toward clinical risk assessment in hypertrophic cardiomyopathy with gadolinium cardiovascular magnetic resonance. *JACC* 2003;41(9):1562-7.
9. Ackerman MJ, VanDriest SL, Ommen SR, et al. Prevalence and age-dependence of malignant mutations in the B – myosin heavy chain and troponin T genes in hypertrophic cardiomyopathy. *JACC* 2002;39(12):2042-8.
10. Shamim W, Yousufuddin M, Wang D, et al. Non-surgical reduction of the interventricular septum in patients with hypertrophic cardiomyopathy. *New Engl J Med* 2002;347(17):1326-33.
11. Sigwart U. Nonsurgical myocardial reduction for hypertrophic obstructive cardiomyopathy. *Lancet* 1995;346:211-4.