

# Ventricular fibrillation induced by rapid atrial rates in patients with hypertrophic cardiomyopathy

M. López Gil<sup>1</sup>, F. Arribas<sup>1</sup> and F. G. Cosío<sup>2</sup>

Cardiology Service, <sup>1</sup>Hospital Universitario 12 de Octubre and <sup>2</sup>Hospital Universitario de Getafe, Madrid, Spain

**Aims** To describe the mechanisms of induction of ventricular fibrillation (VF) by rapid atrial rates in patients with hypertrophic cardiomyopathy (HCM).

**Methods** Electrophysiological studies, management and follow-up in three patients with HCM with VF induced by atrial pacing.

**Results** In one patient, spontaneous sinus tachycardia triggered VF. In another patient, VF occurred after verapamil infusion during rapid atrial fibrillation, and in the remaining patient there was no clinical VF. In all three patients, short runs of atrial pacing (cycle length 272–380 ms) induced VF, and QRS widening preceded fibrillation in all patients. Marked ventricular electrogram fragmentation was documented in one patient during atrial pacing and in another patient during late ventricular extrastimuli. Hypotension was associated with sinus tachycardia in one patient. The two patients developing clinical VF

underwent atrioventricular (AV) junctional ablation; a ventricular defibrillator was implanted in one, and a mode-switching dual-chamber pacemaker in the other. No arrhythmic events occurred during 34- and 35-month follow-up, respectively. In the other patient, postatrial fibrillation pauses caused syncope, and he is asymptomatic 52 months after implantation of a dual-chamber pacemaker.

**Conclusions** Rapid atrial rates can trigger VF in some patients with HCM, probably through a combination of electrophysiological and ischaemic mechanisms. AV junctional ablation may prevent VF in selected cases.

(Europace 2000; 2: 327–332)

© 2000 The European Society of Cardiology

**Key Words:** Hypertrophic cardiomyopathy, ventricular fibrillation, sudden death, syncope, atrioventricular junctional ablation.

## Introduction

Syncope and sudden death are common problems in hypertrophic cardiomyopathy (HCM)<sup>[1]</sup>. The mechanisms responsible can be multiple, ranging from electrophysiological to haemodynamic disturbances<sup>[2,3]</sup>. Multiple electrophysiological abnormalities have been described in this disease, that could produce syncope or sudden death, including sinus node dysfunction, atrioventricular (AV) block, supraventricular tachycardia and ventricular arrhythmias<sup>[3]</sup>. Patients with HCM have a tendency to develop polymorphic ventricular tachycardia or ventricular fibrillation (VF) during electrophysiological testing<sup>[4,5]</sup>, that could be related to abnormal conduction in the myopathic myocardium<sup>[6,7]</sup>. There have been isolated reports of the precipitation

of ventricular tachycardia or fibrillation by atrial fibrillation or atrial stimulation<sup>[5,6,8,9]</sup>.

The present study describes three patients with HCM and syncope, in whom polymorphic ventricular tachycardia leading to VF was induced by atrial stimulation. This was associated in two cases with ventricular electrogram fragmentation at high rates and/or extrastimuli. In one case, it was a proven cause of clinical syncope, and was successfully treated by AV junctional ablation.

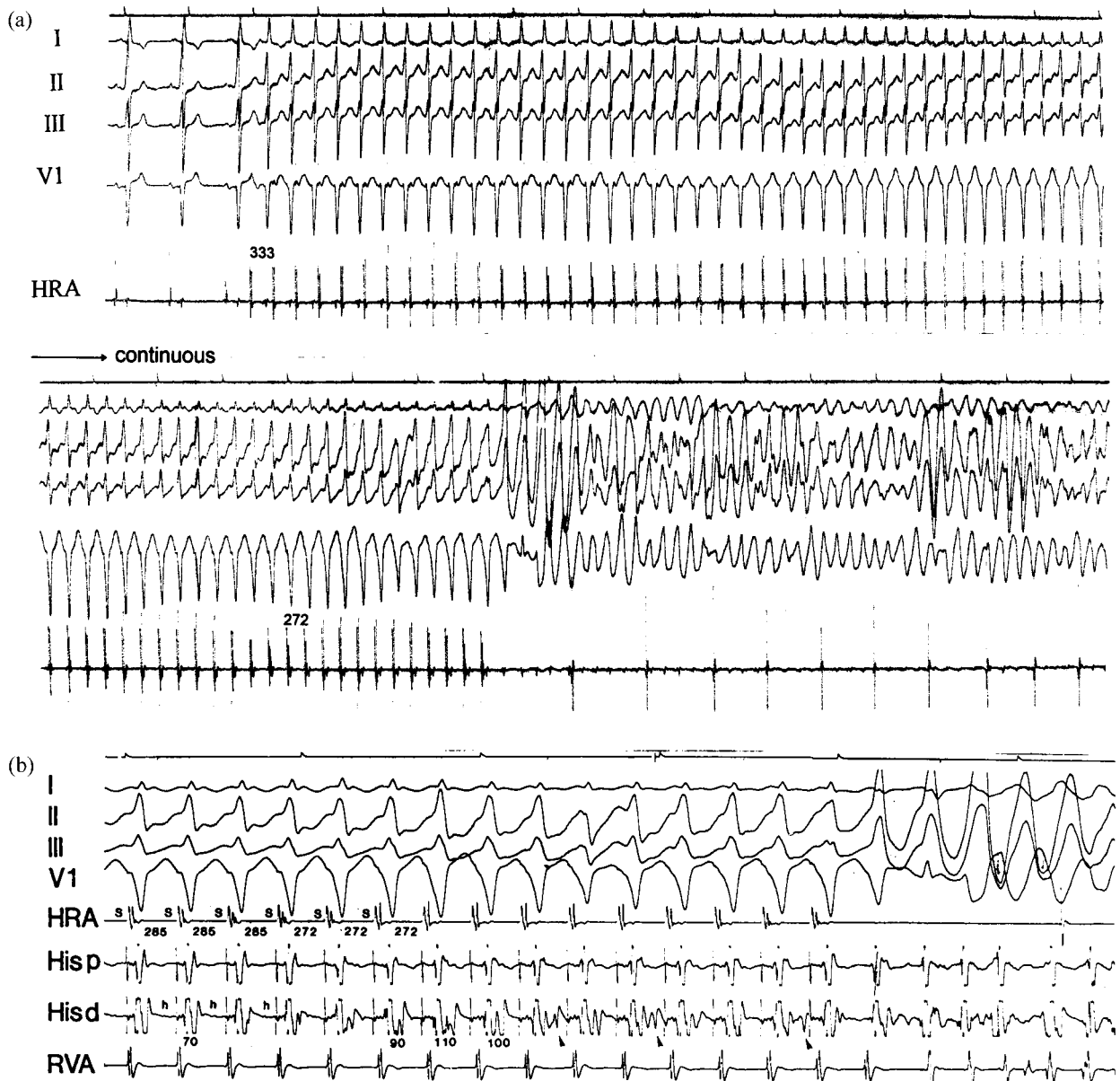
## Case reports

### Patient 1

A 54-year-old male with known HCM, on long-term treatment with propranolol, was evaluated for repetitive syncope in the previous 2 weeks, unrelated to exercise. Physical examination disclosed a grade II/VI systolic murmur. The electrocardiogram (ECG) showed sinus rhythm and left ventricular hypertrophy. A treadmill test produced a normal blood pressure and sinus rate

Manuscript submitted 20 October 1999, revised 21 April 2000, and accepted 2 June 2000.

*Correspondence:* Dr M. López Gil, Servicio de Cardiología, Hospital '12 de Octubre', Carretera de Andalucía, km 5,4, 28041 Madrid, Spain.



**Figure 1** (a) ECG leads I, II, III and V1, and high right atrium (HRA) electrogram during HRA stimulation at progressively shorter cycle length (333–272 ms) with 1:1 AV conduction. QRS widening with ST changes herald the development of ventricular fibrillation (VF). (b) ECG leads I, II, III and V1, and intracardiac recordings from HRA, Hisp and right ventricular apex (RVA) at the time of development of VF (see a). Ventricular electrogram at His becomes widened and fragmented (arrowheads) before fibrillation. H–V interval is 70 ms during pacing (basal 50 ms).

response, without clinical or ECG signs of ischaemia. An echocardiogram demonstrated asymmetrical left ventricular hypertrophy (septum 20 mm), systolic anterior movement of mitral valve with mild mitral regurgitation, and subaortic outflow gradient of 12 mmHg.

Electrophysiological study was performed fasting, and 3 days after stopping propranolol. AH and HV intervals were normal; corrected sinus node recovery time was 570 ms and atrial pacing revealed 1:1 AV conduction at

220 beats  $\cdot$  min<sup>-1</sup> (bpm). After 18 s at this rate, fragmentation of ventricular septal electrogram developed (Fig. 1) with QRS widening and aberration, leading to a syncopal polymorphic ventricular tachycardia needing defibrillation. Atrial fibrillation ensued, with ventricular rate at 150–160 bpm and no QRS widening. Sinus pauses of 3–7 s and recurrent atrial fibrillation followed cardioversion, requiring right atrial pacing and intravenous procainamide for sinus rhythm stability. Ventricular stimulation was not performed. The next day,



**Figure 2** ECG leads I, II, III and VI, and intracardiac recordings from high right atrium (HRA), His (proximal and distal) and right ventricular apex (RVA) during runs of polymorphic ventricular tachycardia induced by spontaneous sinus tachycardia in patient 2. His deflection is marked (h).

atrial fibrillation occurred spontaneously, followed by near-syncope sinus pauses upon spontaneous termination. A dual-chamber pacemaker was implanted, and the patient remains asymptomatic, 4 years later, on propranolol.

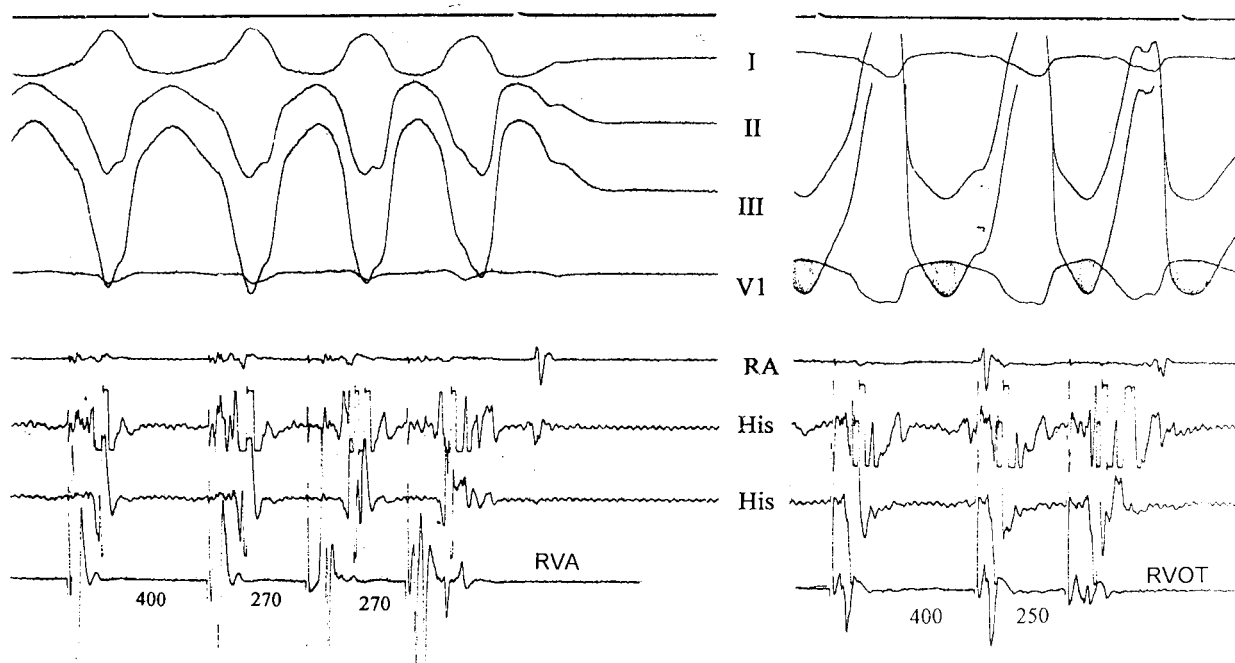
### Patient 2

An 18-year-old female with non-obstructive HCM was studied for episodes of effort-related dizziness progressing to syncope. She had dyspnoea, palpitations and mild chest pain with mild-to-moderate effort despite 50 mg atenolol daily. Physical examination disclosed a fourth heart sound and a II/VI systolic murmur. The ECG showed sinus rhythm and left ventricular hypertrophy with incomplete left bundle branch block. Years before, the ECG had shown prominent septal Q waves. An echocardiogram disclosed severe asymmetric left ventricular hypertrophy involving the septum and anterolateral wall, and normal systolic function. There was mild systolic anterior movement of the anterior mitral leaflet, and mild mitral regurgitation.

In hospital, monitoring showed sinus bradycardia (35 bpm) at rest and marked sinus tachycardia with rate-dependent left bundle branch block triggered by emotion or minor effort. Hypotension often occurred during tachycardia. A tilt test produced sinus tachycardia with left bundle branch block and severe symptomatic hypotension. A treadmill test could not be carried out because she developed sinus tachycardia with left bundle branch block and hypotension during preparation.

Electrophysiological study was performed 3 days after stopping atenolol. Baseline AV conduction was normal but there was left bundle branch block during atrial pacing at rates  $\geq 100$  bpm. Spontaneous sinus tachycardia produced left bundle branch block and short runs of polymorphic ventricular tachycardia (Fig. 2). During atrial pacing at 130 and 140 bpm, there was 1:1 AV conduction and runs of non-sustained polymorphic ventricular tachycardia. Atrial pacing at 160 bpm resulted in VF requiring DC shock. Single atrial extrastimuli during atrial drive pacing (cycle 600 ms) disclosed no abnormalities. Both at the right ventricular apex and outflow tract, single and double extrastimuli produced marked ventricular electrogram fragmentation with coupling intervals  $\geq 250$  ms (Fig. 3). Double and triple extrastimuli triggered non-sustained polymorphic ventricular tachycardia from the right ventricular apex and VF from the outflow tract. Ventricular fibrillation was again induced by atrial pacing at 160 bpm after intravenous infusion of propranolol  $0.2 \text{ mg} \cdot \text{kg}^{-1}$ .

Spontaneously, 2 days after the procedure, on atenolol 50 mg daily, emotional sinus tachycardia resulted in progressive QRS widening leading to VF. Fibrillation terminated spontaneously after 96 s, leading to asystole for 10 s, then a slow ventricular rhythm and, finally, sinus rhythm. The patient lost consciousness during the event. Radiofrequency ablation of the AV junction was performed and a ventricular automatic defibrillator was implanted; the patient remaining dependent on VVI pacing by the defibrillator (dual-chamber pacing devices were not available at that time). During 31 months of follow-up, the patient has not suffered tachyarrhythmic events.



**Figure 3** ECG leads I, II, III and V1, and intracardiac recordings from high right atrium (HRA), His (proximal and distal) and right ventricular (RV) in patient 2. Left panel shows that double extrastimuli at the RV apex (RVA) with relatively long coupling intervals produce widening and fragmentation of the apical and septal (His) ventricular electrograms. Right panel shows that a single extrastimulus at the RV outflow tract (RVOT) produced a similar effect. Ventricular effective refractory period was 250 ms at RVA and 230 ms at RVOT.

### Patient 3

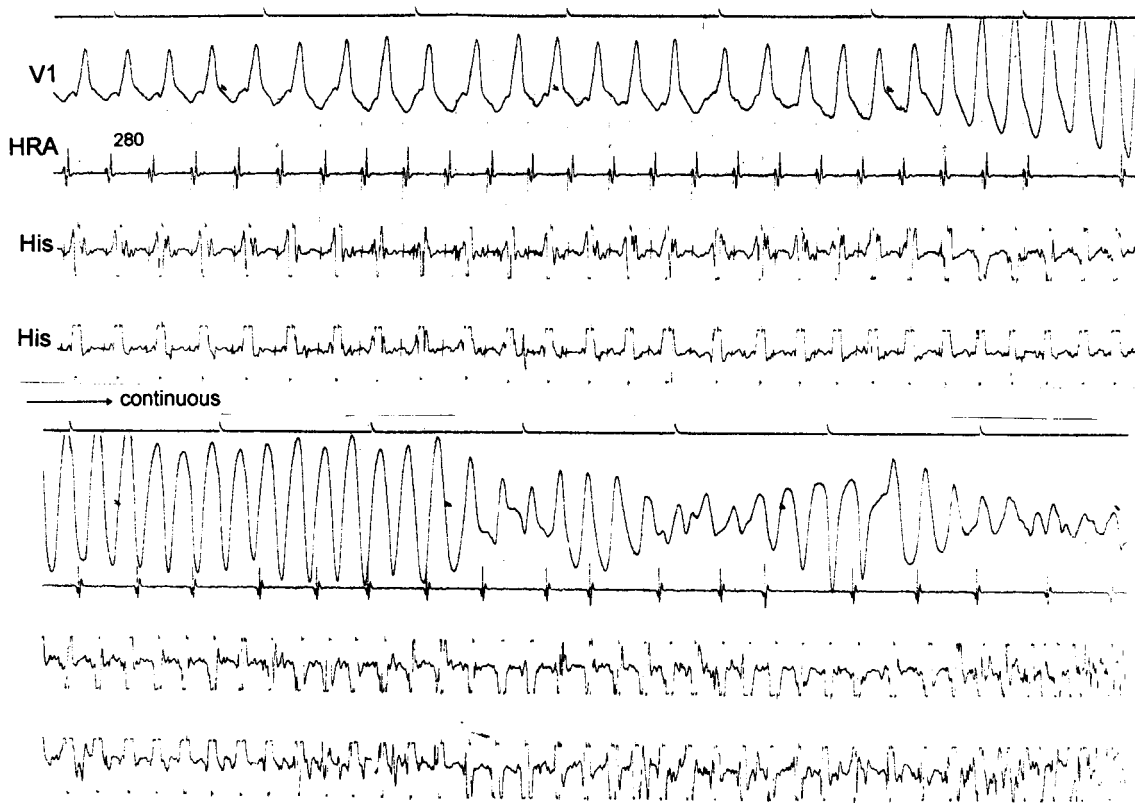
A 60-year-old female with non-obstructive HCM, treated with 100 mg of atenolol daily, came to the emergency room because of chest pain and atrial fibrillation with ventricular rate 180–200 bpm. Physical examination showed blood pressure 140/80 mmHg and no heart murmurs. Intravenous verapamil (5 mg) did not slow heart rate and was followed by VF. After defibrillation, she remained stable in sinus rhythm. The ECG showed severe left ventricular hypertrophy. An echocardiogram disclosed symmetrical left ventricular hypertrophy (16 mm), mild mitral regurgitation, no left ventricular outflow gradient and normal atrial size. Six months previously, a treadmill test showed a normal heart rate and blood pressure response, and was negative for myocardial ischaemia. At heart catheterization, the coronary arteries were normal. The left ventricle was severely hypertrophic with systolic cavity obliteration. There was mild mitral regurgitation but no outflow gradient.

An electrophysiological study was performed 7 days after stopping atenolol. AV conduction was normal apart from right bundle branch block due to catheter manipulation. Atrial pacing at 214 bpm with 1:1 AV conduction resulted in further QRS widening, followed by polymorphic ventricular tachycardia and VF (Fig. 4). Up to three extrastimuli during three differing ventricular paced rates at the right ventricular apex and the outflow tract failed to induce ventricular arrhythmias.

AV nodal conduction was interrupted by radiofrequency ablation, and a dual-chamber pacemaker with automatic mode switch was implanted. After 30 months of follow-up, the patient is mildly symptomatic with exertional chest pain, on treatment with atenolol. There have been no further episodes of atrial fibrillation.

### Discussion

These observations in three patients illustrate an unusual, albeit previously described<sup>[4-6,8-10]</sup>, arrhythmogenic mechanism capable of causing sudden death in HCM. In all three of these patients, a supraventricular tachycardia induced polymorphic ventricular tachycardia and VF. In one patient, this was only precipitated during electrophysiological study, and the symptoms that appeared to be related to bradycardia were treated successfully with a DDD pacemaker. However, in the other two patients, there was spontaneous clinical documentation of the event, during sinus tachycardia in patient 2, and after verapamil administration for rapid atrial fibrillation in patient 3. Therapeutic interruption of AV conduction resulted in lack of recurrence of ventricular arrhythmia in both. Findings during electrophysiological study were very similar in all three cases. Rapid AV conduction resulted in QRS widening followed by polymorphic ventricular tachycardia and VF. Rapid atrial rates resulted in a severe disturbance in intraventricular conduction, leading to disorganization



**Figure 4** ECG lead V1 and intracardiac recordings from high right atrium (HRA) and His during atrial stimulation with 1:1 atrioventricular conduction, cycle length 280 ms, inducing polymorphic ventricular tachycardia and ventricular fibrillation in patient 3. Note QRS widening in the last conducted beats preceding polymorphic ventricular tachycardia.

of ventricular rhythm, an unusual event except in Wolff-Parkinson-White syndrome, where extremely fast ventricular rates are possible in atrial fibrillation<sup>[11]</sup>.

Supraventricular tachycardias are common in HCM<sup>[12-14]</sup> and several factors may make these patients susceptible to VF in the absence of pre-excitation: (1) abnormal conduction in myopathic myocardium; (2) a 'superconductor' AV node; and (3) haemodynamic instability with myocardial ischaemia. Intraventricular conduction disturbances are frequent in HCM, and some conduction abnormalities are peculiar to this disease. The abnormally deep Q waves commonly seen in HCM, often attributed to septal hypertrophy, tend to decrease in size or disappear with atrial pacing or atrial extrastimuli<sup>[15]</sup>. Inhomogeneous ventricular refractoriness has been described, as well as marked fragmentation of ventricular electrograms by extrastimuli, especially in patients with a history of resuscitated sudden death or VF<sup>[6,7,16]</sup>. Another manifestation of abnormal intraventricular conduction may be the easy induction of polymorphic ventricular tachycardia with programmed ventricular stimulation<sup>[5,17]</sup>, a phenomenon also related to a history of cardiac arrest<sup>[2,4,6]</sup>. In keeping with this mechanism is the demonstration in two of the present cases of marked fragmentation of ventricular electrograms during rapid regular atrial pacing (patient

1) or ventricular extrastimuli with relatively long coupling intervals (patient 2).

A 'superconductor' AV node is relatively common in HCM<sup>[2]</sup>. In the presence of supraventricular tachycardia, this may result in very fast ventricular rates, capable of precipitating abnormal intraventricular conduction. Patients 1 and 3 did have 1:1 AV conduction at rates above  $200 \text{ min}^{-1}$ , and one of them developed VF during rapidly conducted atrial fibrillation.

Other authors have attributed VF to hypotension and/or ischaemia during supraventricular tachycardia<sup>[4,6,8,9,18]</sup> and an abnormal blood pressure response during exercise has been related to the risk of sudden death<sup>[19]</sup>. Intraarterial pressures were not monitored in the present study, and hypotension can not be ruled out; however, pacing runs were probably too short to produce significant ischaemia. Furthermore, patient 2 showed fragmentation of ventricular electrograms and VF with relatively late extrastimuli; a situation unlikely to produce ischaemia. On the other hand, in patient 3, in whom clinical VF was precipitated by verapamil infusion, it is possible that hypotension played a role.

An interesting clinical consequence of these observations is the possible benefit of AV junctional ablation to prevent ventricular arrhythmia episodes (and perhaps hypotension) in selected patients with HCM and a

history of syncope or aborted sudden death. Electrophysiological study protocol in these patients should include incremental atrial pacing, and perhaps induction of atrial fibrillation. The prevention of fast AV conduction, even at the cost of AV dissociation, completely abolished syncopal episodes and ventricular arrhythmias in patient 2, and may have contributed to the stable clinical course in patient 3. In some of these patients, AV junctional ablation could make implantation of an automatic defibrillator unnecessary, or at least prevent unnecessary discharges, if defibrillator implantation is considered safer. Along these lines, it could also be considered that control of AV conduction with amiodarone might be useful in selected patients. In patients 2 and 3, it was considered that AV ablation offered a better guarantee in view of the clinical presentation with VF.

## References

- [1] Maron BJ, Fananapazir L. Sudden cardiac death in hypertrophic cardiomyopathy. *Circulation* 1992; 85(Suppl I): 57-63.
- [2] Fananapazir L, Tracy CM, Leon ML, *et al.* Electrophysiologic abnormalities in hypertrophic cardiomyopathy: a consecutive analysis in 155 patients. *Circulation* 1989; 80: 1259-68.
- [3] Frenneaux MP, Counihan PJ, Caforio ALP, Chikamori T, McKenna WJ. Abnormal blood pressure response during exercise in hypertrophic cardiomyopathy. *Circulation* 1990; 82: 1995-2002.
- [4] Fananapazir L, Epstein SE. Hemodynamic and electrophysiologic evaluation of patients with hypertrophic cardiomyopathy surviving cardiac arrest. *Am J Cardiol* 1991; 67: 280-7.
- [5] Kuck K-H, Kunze KP, Schluter M, Nienaber CA, Costard A. Programmed electrical stimulation in hypertrophic cardiomyopathy. Results in patients with and without cardiac arrest or syncope. *Eur Heart J* 1988; 9: 177-85.
- [6] Watson RM, Schartz JL, Maron BJ, Tucker E, Rosing DR, Josephson ME. Inducible polymorphic ventricular tachycardia and ventricular fibrillation in a subgroup of patients with hypertrophic cardiomyopathy at high risk for sudden death. *J Am Coll Cardiol* 1987; 10: 761-74.
- [7] Saumarez RC, Camm AJ, Panagos A, *et al.* Ventricular fibrillation in hypertrophic cardiomyopathy is associated with increased fractionation of paced right ventricular electrograms. *Circulation* 1992; 86: 467-74.
- [8] Stafford WJ, Trhoman RG, Bilsker M, Zaman L, Castellanos A, Myerburg RJ. Cardiac arrest in an adolescent with atrial fibrillation and hypertrophic cardiomyopathy. *J Am Coll Cardiol* 1986; 7: 701-4.
- [9] Favale S, Di Biase M, Rizzo U, Minafra F, Rizzon P. Ventricular fibrillation induced by transesophageal atrial pacing in hypertrophic cardiomyopathy. *Eur Heart J* 1987; 8: 912-6.
- [10] Madariaga I, Carmona JR, Mateas FR, Lezaun R, de los Arcos E. Supraventricular arrhythmia as the cause of sudden death in hypertrophic cardiomyopathy. *Eur Heart J* 1994; 15: 134-7.
- [11] Klein G, Bashore TM, Sellers TD, Pritchett EL, Smith WM, Gallagher JJ. Ventricular fibrillation in the Wolff-Parkinson-White syndrome. *N Engl J Med* 1979; 301: 1080-5.
- [12] Brembilla-Perrot B, Terrier de la Chaise A, Beurrier D. La fibrillation auriculaire paroxystique: principale cause de syncope dans la cardiomyopathie hypertrophique? *Arch Mal Coeur Vaiss* 1993; 86: 1573-8.
- [13] Schiavone VA, Maloney JD, Lever HM, Castle LW, Sterba R, Morant V. Electrophysiologic studies of patients with hypertrophic cardiomyopathy presenting with syncope of undetermined etiology. *Pacing Clin Electrophysiol* 1986; 9: 476-81.
- [14] Brembilla-Perrot B, Beurrier D, de la Chaise AT, *et al.* Significance and prevalence of inducible atrial tachyarrhythmias in patients undergoing electrophysiologic studies for presyncope or syncope. *Int J Cardiol* 1996; 53: 61-9.
- [15] Cosio FG, Moro C, Sáenz de la Calzada C, Llovet A. The Q waves of hypertrophic cardiomyopathy. An electrophysiologic study. *N Engl J Med* 1980; 302: 96-9.
- [16] Saumarez RC, Slade AK, Grace AA, Sadoul N, Camm AJ, McKenna WJ. The significance of paced electrogram fractionation in hypertrophic cardiomyopathy: A prospective study. *Circulation* 1995; 91: 2762-8.
- [17] Wellens H, Brugada P, Stevenson WG. Programmed electrical stimulation of the heart in patients with life threatening arrhythmias: what is the significance of induced arrhythmias and what is the correct stimulation protocol? *Circulation* 1985; 72: 1-7.
- [18] Fananapazir L, Chang AC, Epstein SE, McAreavey D. Prognostic determinants in hypertrophic cardiomyopathy. Prospective evaluation of a therapeutic strategy based on clinical, holter, hemodynamic and electrophysiological findings. *Circulation* 1992; 86: 730-40.
- [19] Sadoul N, Prasad K, Elliott PM, Bannarjee S, Frenneaux MP, McKenna WJ. Prospective prognostic assessment of blood pressure response during exercise in patients with hypertrophic cardiomyopathy. *Circulation* 1997; 96: 2987-91.