Case Reports

Sustained Ventricular Tachycardia Responsive to Verapamil in Patients with Hypertrophic Cardiomyopathy

Clinical and Electrophysiological Assessment of Drug Efficacy

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SUMMARY

Recently, we examined 2 cases of hypertrophic cardiomyopathy (HCM) presenting with sustained ventricular tachycardia (VT). One case was a 62 year old male with midventricular hypertrophy and monomorphic sustained VT. After admission, the efficacies of procainamide, disopyramide, aprindin, flecainide, mexiletine and verapamil were evaluated by means of continuous electrocardiographic monitoring. Verapamil prevented the recurrence of sustained VT and markedly reduced the frequency and number of runs of nonsustained VT. In the electrophysiologic study, rapid VT was induced by double extrastimuli at the right ventricular apex. Intravenous verapamil at a dose of 10 mg prevented the induction of VT. The patient was discharged on verapamil and remains asymptomatic after 3 months of follow up. The other case was a 34 year old female who was a survivor of cardiac arrest. Monomorphic VT was observed on emergency admission and was converted to sinus rhythm by direct current cardioversion after resuscitation. In the electrophysiologic study, rapid VT was induced by double extrastimuli at the right ventricular outflow tract. Verapamil at a dose of 10 mg prevented the induction of VT. These 2 cases of HCM are rare in that they presented with sustained VT. It is also of interest that verapamil, which has been used conventionally in HCM, prevented VT.

Additional Indexing Words:
Cardiac arrest  Sudden death  Electrophysiologic study
In patients with hypertrophic cardiomyopathy (HCM), nonsustained ventricular tachycardia (VT) is not an uncommon finding and is associated with a high risk of sudden cardiac death.\textsuperscript{1,2} It is unknown, however, whether or not abolition of this arrhythmia would improve prognosis.\textsuperscript{3-5} On the contrary, sustained VT in HCM is rare.\textsuperscript{3} We recently saw 2 cases and were able to evaluate sustained VT by continuous electrocardiographic monitoring and electrophysiologic study.

**Case Report**

Case 1: A 62 year old man was referred to our hospital for the management of recurrent sustained VT. His mother and 3 of his 9 siblings had died suddenly and his 2 sons were diagnosed as having HCM. He was found to have abnormal electrocardiographic (ECG) findings at the age of 52. He had an episode of lacunar cerebral infarction 6 years later, when he was diagnosed as having HCM and received oral therapy with propranolol (30 mg/day) plus verapamil (120 mg/day) thereafter. Ambulatory ECG showed couplets of ventricular extrasystole but he had been asymptomatic until 5 days before admission because of palpitations and chest pain. On admission, the ECG showed sustained monomorphic VT with a rate of 180 to 190 beats/min (Fig. 1). The QRS configuration was a right bundle branch block with an abnormal right axis deviation pattern. The physical examination

![Fig. 1. Electrocardiogram during sinus rhythm (Panel A) and ventricular tachycardia (Panel B) in case 1.](image_url)
during sinus rhythm was unremarkable; blood pressure was 146/82 mmHg, and heart and lungs were normal to auscultation. Blood chemistry and peripheral blood count were normal except for signs of mild liver dysfunction. There were no inflammatory signs. A chest X-ray showed no abnormality. Resting ECG showed normal frontal axis (+45°) and left ventricular hypertrophy with negative T waves in leads I, II, III, aV_{L}, aV_{R} and V_{4} to V_{6} (Fig. 1). The time intervals for QT and QTc were 0.44 and 0.46 sec, respectively. On cardiac catheterization, left ventricular pressure was 193/8 mmHg, and end-diastolic pressure 24 mmHg. There was no pressure gradient across the left ventricular outflow tract, but the left ventriculogram showed midventricular hypertrophy of the left ventricle and akinesis of the apex. The left ventricular ejection fraction was 61%. Coronary angiography showed no fixed stenosis.

**Serial drug testing by means of electrocardiographic monitoring:** The patient underwent serial drug testing while he was monitored by a continuous ECG recorded at a paper speed of 5 mm/sec. Before starting oral antiarrhythmic therapy, sustained VT recurred several times a day. Administration of each drug was continued for 5 days or longer. The duration, rate and frequency of the nonsustained VT of the same morphology as that of the sustained VT were analyzed. If sustained VT recurred, the antiarrhythmic drug was considered ineffective and was stopped. “Sustained VT” was defined as VT lasting more than 30 sec or requiring pacing or cardioversion for termination. “Nonsustained VT” was defined as VT that lasted more than 3 beats and terminated spontaneously within 30 sec.

Table I summarizes the results of the drug testing. Propranolol at a dose of 15 to 30 mg per day was continued throughout the drug testing. Terminati-

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage (mg/day)</th>
<th>Plasma level* (ng/ml)</th>
<th>SVT**</th>
<th>NSVT 3-14</th>
<th>NSVT &gt;15 beats</th>
<th>VT rate (beats/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procainamide</td>
<td>3000</td>
<td>5.4</td>
<td>+</td>
<td>#</td>
<td>-</td>
<td>165</td>
</tr>
<tr>
<td>Disopyramide</td>
<td>500</td>
<td>2.2</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>155-175</td>
</tr>
<tr>
<td>Flecaïnid</td>
<td>300</td>
<td>~</td>
<td>~</td>
<td>#</td>
<td>-</td>
<td>165-185</td>
</tr>
<tr>
<td>Aprindine</td>
<td>80</td>
<td>~</td>
<td>~</td>
<td>#</td>
<td>~</td>
<td>150</td>
</tr>
<tr>
<td>Mexiletine</td>
<td>400</td>
<td>~</td>
<td>+</td>
<td>#</td>
<td>+</td>
<td>170</td>
</tr>
<tr>
<td>Verapamil</td>
<td>320</td>
<td>~</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>110-155</td>
</tr>
</tbody>
</table>

SVT = sustained ventricular tachycardia; NSVT = nonsustained ventricular tachycardia.

* Plasma level at the time of recurrence of ventricular tachycardia or trough level before the next dose.

** Frequency is expressed as follows: ~ = absent, + = one to 10 episodes per day, ++ = 11 to 100 episodes per day, ### = more than 101 episodes per day.
tion of the VT was possible by injection of 200 mg of procainamide. But procainamide, disopyramide and mexiletine could not prevent the recurrence of sustained VT in spite of therapeutic plasma levels. Flecainide at a dose of 300 mg daily or aprindine at a dose of 80 mg daily suppressed sustained VT, however nonsustained VT appeared frequently. Verapamil, at doses of 320 to 360 mg a day, suppressed sustained VT completely and markedly reduced the frequency of nonsustained VT.

Electrophysiologic study: Possible risks and complications of this test were explained to the patient and his family, and informed consent was obtained before the electrophysiologic study. Drugs had been withdrawn 4 days before the study. The protocol of the electrophysiologic study has been described previously.\textsuperscript{6}-\textsuperscript{8}) In the control study, the effective refractory period (ERP) of the right ventricular apex was 200 msec at the basic cycle length (BCL) of 400 msec. Rapid VT with a cycle length of 200 to 220 msec was induced by a double extrastimuli delivered at the right ventricular apex, and soon degenerated into ventricular fibrillation which required electrical cardioversion (Fig. 2). The VT was induced without critical prolongation of the local ventricular electrogram at the pacing site. The morphology of the first beat of the VT was similar to that of clinical monomorphic VT. Verapamil

![Fig. 2. Rapid ventricular tachycardia induced by double ventricular extrastimuli in case 1. Surface leads in I, II and V\textsubscript{1} are shown with intracavitary electrogram from the right ventricular apex (RVA). Following ventricular pacing (S\textsubscript{1}-S\textsubscript{1}) at a cycle length of 500 msec, double extrastimuli (S\textsubscript{2}S\textsubscript{3}) with an interval of 240, 180 msec induced a rapid ventricular tachycardia with cycle length of 200 to 220 msec. The local ventricular electrogram at the pacing site following the last extrastimulus was 140 msec in duration. Ventricular tachycardia degenerated into ventricular fibrillation and required electrical cardioversion.](https://example.com/fig2)
at a dose of 10 mg was administered intravenously. The ERP of the right ventricular apex became 220 msec at the BCL of 400 msec. VT became non-inducible from the right ventricular apex, the outflow tract of the right ventricle and from the left ventricle by our full protocol (Fig. 3). The patient was discharged on 320 mg/day of verapamil and the follow up period of 7 months has been uneventful.

Case 2: A 34 year old woman was referred to our hospital for the assessment of sustained VT. Her father had been diagnosed as having HCM and was treated medically. She was seen to have right bundle branch block on ECG 2 months before admission but was asymptomatic. She suddenly lost consciousness in the office and was admitted to the hospital by ambulance. On admission, she was in cardiac arrest. Cardiopulmonary resuscitation was performed promptly. Electrocardiographic monitoring showed ventricular

![Programmed ventricular stimulation after verapamil in case 1.](image)

**Fig. 3.** Programmed ventricular stimulation after verapamil in case 1. Panel A: Double ventricular extrastimuli or rapid ventricular pacing at the right ventricular apex did not induce VT after verapamil. Panel B: VT was not inducible even at the left ventricle after verapamil.
fibrillation. VT appeared soon after direct current cardioversion, as shown in Fig. 4, but was successfully converted to sinus rhythm after several attempts. Spontaneous respiration appeared thereafter and she was admitted to a coronary care unit. One month later she had recovered without sequelae and was referred to our hospital for the management of VT.

Resting ECG showed right bundle branch block with deep Q waves in leads I, aVL, V4 to V6. Two weeks after cardiac arrest, the right bundle branch block disappeared on normal sinus rhythm, but appeared in a rate-dependent manner; it developed at a rate faster than 130 bpm on treadmill exercise testing. Echocardiography revealed typical findings of HCM; asymmetric septal hypertrophy and systolic anterior motion of the mitral valve were observed. Wall thickness of the interventricular septum and posterior wall of the left ventricle was 21 and 8 mm, respectively. On cardiac catheterization, left ventricular end-diastolic pressure was 23 mmHg. There was no pressure gradient in the left ventricle even after the introduction of extrasystoles or isoproterenol infusion. Left ventricular ejection fraction was 73%. Coronary angiography showed no fixed stenosis.

Electrophysiologic study: After informed consent was obtained, she underwent an electrophysiologic study in the drug-free state. In the control study, the ERP of the right ventricular outflow tract was 280 and 240 msec at a BCL of 600 and 400 msec, respectively. Rapid, polymorphic nonsustained VT was induced by double extrastimuli at the right ventricular outflow tract (Fig. 5). A more aggressive mode of VT induction was no longer tried. After intravenous administration of verapamil at a dose of 10 mg, the ERP of the right ventricular outflow tract became 240 and 200 msec at a BCL of 600 and 400 msec, respectively, and VT became noninducible even from the left ventricle. She is now asymptomatic on chronic therapy with verapamil.
Fig. 5. Ventricular tachycardia induced in the electrophysiologic study in case 2. Panel A: Rapid, polymorphic nonsustained ventricular tachycardia was induced by double extrastimuli at the right ventricular outflow tract. Panel B: After intravenous verapamil at a dose of 10 mg, ventricular tachycardia became noninducible at the right and left ventricles.

DISCUSSION

Sudden death in patients with HCM is not uncommon\(^9\)-\(^12\) and its cause is generally considered to be ventricular tachyarrhythmias.\(^1\),\(^2\),\(^13\) However, sustained VT is rarely observed in patients with HCM.\(^3\) Therefore, the present cases are very interesting in considering the nature of VT in HCM.

In case 1, we were able to evaluate the efficacy of antiarrhythmic drugs for VT by continuous electrocardiographic monitoring. Verapamil prevented sustained VT completely. The number of runs, rate, and frequency of nonsustained VT were reduced significantly. Verapamil also prevented the induction of VT in the electrophysiologic study. The induced VT was very rapid and the QRS configuration of VT seemed to be different from the clinical VT. Whether this rapid VT could be converted to monomorphic VT by the administration of antiarrhythmic drugs was not tested at various doses.

In case 2, sustained monomorphic VT observed after defibrillation was the most likely cause of cardiac arrest. She had cardiac arrest as the first symptom, as is sometimes the case with HCM. Verapamil prevented the induction of rapid VT. However, verapamil shortened the ERP of the right ventricular outflow tract, which seemed to be prolonged in the control state.

In both cases, the induced VT was rapid, and polymorphic. The significance of induced polymorphic VT in patients presenting with sustained monomorphic VT or in those with cardiac arrest remains unclear. Stevenson and Wellens et al\(^14\) considered it to be a nonspecific finding related to an
aggressive pacing protocol. On the other hand, Horowitz et al\textsuperscript{15}) analyzed 21 patients who had polymorphic VT in the absence of electrolyte disturbance, antiarrhythmic drug therapy or acute ischemia and showed that 1) polymorphic VT was reproducibly induced in 19 of 21 patients and was organized into a monomorphic sustained VT in 3 of them; 2) in 8 patients, monomorphic sustained VT was initiated by the same stimulation protocol as the control study after administration of class Ia antiarrhythmic agents; 3) in 2 of the 8 patients, the origin of VT was determined and resected surgically, resulting in noninducibility of both monomorphic VT and polymorphic VT. These data strongly suggest that the induced polymorphic VT is a rapid VT originating from the same origin as the clinical monomorphic VT with a changing exit site. So, induced polymorphic VT should be interpreted with caution in individual cases.

In case 1, VT was induced with the local ventricular electrogram at the pacing site being almost normal (140 msec in duration). This contrasted with other induced polymorphic VT in HCM at our institute, in which the local ventricular electrogram was prolonged to 215 to 400 msec at the time of the induction of VT (authors, unpublished data). In addition, the similarity of the morphology of the first beat of the VT might suggest that rapid VT related to clinical VT was induced and degenerated into ventricular fibrillation, but it is only an assumption because we did not test whether or not the induced polymorphic VT converted into monomorphic VT after administration of a class I antiarrhythmic drug. In case 2, the relation between the induced polymorphic VT and the clinical sustained VT was not clear.

This report confirmed that verapamil prevented both clinical and induced sustained VT. Our results differ from a report by McKenna et al, in which the ineffectiveness of verapamil in suppressing nonsustained VT in patients with HCM is described.\textsuperscript{16}) The mechanism of drug efficacy is unknown, but in addition to causing a prolongation of ERP, verapamil may slow the conduction velocity in the reentrant circuit if it contains slow fibers\textsuperscript{17}) or it may inhibit the delayed after-depolarization.\textsuperscript{18})

The present study showed that the selection of regimens guided by electrophysiologic study was useful in at least one patient with HCM complicated by sustained VT. A long-term follow up will be needed to ascertain if such therapy prevents sudden cardiac death.

\textbf{References}

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