Catheter Ablation of Reentrant Left Ventricular Tachycardia Associated with Fabry disease: A Case Report

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A 51-year-old man, who was diagnosed with Fabry disease resulting from a kidney biopsy for proteinuria and renal failure in 2002, was admitted to our hospital for sustained ventricular tachycardia (VT). In the electrophysiological study, VT (cycle length: 310 ms) was successfully induced by right ventricle programmed stimulation and the twelve-lead electrocardiogram showed a right bundle branch block configuration with right axis deviation. The mechanism of the VT was considered to be reentry by entrainment phenomenon. An electro-anatomical mapping system identified a low voltage area located close to the left ventricular anterior-apical wall. During VT an isolated pre-potential was recorded 42 ms prior to the QRS onset near the border zone which was located between the low and normal voltage areas. At this mapping site entrainment with fusion and a post-pacing interval that matched the VT cycle length were observed. A radiofrequency energy delivery at this site terminated the VT after 35 seconds. The entrainment mapping could be useful for identifying a critical reentry circuit path. This case is the first description of reentrant VT originating from the thickened left ventricular wall in a patient with Fabry disease.

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Introduction

Fabry disease (an alpha galactosidase A deficiency) is an X-linked hereditary disorder leading to the pathological accumulation of globotriaosylceramide (GL-3) in lysosomes, particularly in the vascular endothelium of the kidney, heart and brain. Recent data suggest that 60% of Fabry disease patients have cardiac symptoms, including palpitation and syncope; however, patients with sustained ventricular tachycardia (VT) are rare.1) We report a case of Fabry disease with sustained reentrant VT. In this case, the VT reentry circuit could be identified by entrainment mapping and an electro-anatomical mapping (CARTO) during electrophysiological study (EPS). The VT terminated with radiofrequency (RF) ablation. To the best of our knowledge, this report describes for the first time VT that originates from a thickened left ventricular (LV) wall that is based on a reentrant mechanism.
Case report

A 51-year-old man presented to our hospital with palpitations. His mother and uncle (mother’s younger brother) had Fabry disease and died of renal failure. In 1993, the results of a health checkup indicated he had electrocardiographic abnormalities, ventricular hypertrophy and proteinuria. In 2002, he was diagnosed as having Fabry disease based on his family history, the enzyme activity, and the results of a kidney biopsy and genetic evaluation. Enzyme replacement therapy (ERT; agalsidase beta, Fabrazyme® 1 mg/Kg every two weeks) with α-GAL A was initiated in May of 2004. As he had no cardiac symptoms except for LV hypertrophy, he annually underwent electrocardiography (ECG) and echocardiography. However, he started to complain of short-lasting palpitations in March of 2007 and their frequency gradually increased. On the 20th of September, 2007, he was transferred to our hospital by ambulance with sustained palpitations. On arrival, his conscious level was clear and blood pressure was 102/60 mmHg. The ECG on admission revealed sustained VT, with a right bundle branch block configuration, right axis deviation, inferior axis, and a heart rate of 194 bpm (Figure 1A). Intravenous lidocaine of 100 mg restored sinus rhythm, however the effect was transiently. He was admitted to our hospital for treatment of VT. The signal-averaged ECG showed positive ventricular late potentials prior to administering any anti-arrhythmic drugs. M-mode, 2-dimensional, and doppler echocardiography were performed. The patient showed a normal ejection fraction (EF) (68%). End-diastolic thickness of the posterior wall was 11.0 mm, and maximal LV wall thickness was 20.5 mm in the septal area. There was no dilatation of the LV (LVDd = 50 mm, LVDs = 31 mm). Figures 1B and 1C show the magnetic resonance image (MRI). A gradient-echo MRI revealed a remarkably thickened LV septal wall and thinned LV apex (Figure 1B). Furthermore, a T2-weighted MRI scan revealed an area with a partially high signal intensity in the basal epicardium and antero-septal endocardium, which suggested there

Figure 1
A) Clinical ventricular tachycardia (VT) morphology on admission
B) Magnetic Resonance Image (MRI): gradient echo sequence
C) MRI: T2-weighted image
was ischemia, edema or myocardial degeneration (Figure 1C). After written informed consent was obtained from the patient and his family, several catheterization studies were performed. Coronary angiography revealed no significant stenosis. Right ventricle (RV) endomyocardial biopsy specimens, which were stained with hematoxylin and eosin, exhibited diffuse sarcoplasmic vacuolar degeneration. An electron microscope image identified typical lysosomal inclusions with a concentric lamellar configuration, the so-called Zebra body, in the myocardial cells. An EPS, endocardial catheter mapping and RF ablation were performed to clarify the onset mechanism and eliminate the VT. Electrode catheters (AF Division, St. Jude Medical, Minnesota, MN, USA) were inserted from the femoral vein into the right ventricular (RV) apex, right atrium (5-Fr. 5 pole catheter) and His bundle region (5-Fr. 6 pole catheter). A CardioLab (General Electric Company, Schenectady, NY, USA) was used to record the 12-lead body surface ECG and intracardiac electrograms at 100 to 200 mm/sec.

Classic entrainment criteria, including constant fusion and progressive fusion, were demonstrated by rapid pacing from the RV apex during the VT, suggesting that the mechanism of VT was reentry with an excitable gap (Figure 3A).

Induced VT cycle length ranged from 290 ms to 310 ms and it remains possible that VT changed to become hemodynamically unstable. Pace mapping was used to define potential exit sites along the border of low-voltage region in the LV anteropolar wall. A perfect pace map could not been obtained anywhere in the endocardium. Induced sustained VT by double extra stimulation from the RV apex was the same QRS morphology as the clinical arrhythmia. Not only voltage map during sinus rhythm but also activation map during VT were constructed using the CARTO system (Biosense Webster Inc., Diamond Bar, CA, USA) (Figure 2A). A MRI indicated that there was a thin wall which corresponded to a low voltage area.

RF energy, which was set at 50 Watts, with a duration of 60 seconds and maximal temperature of 60°C, was delivered using a 4 mm-tip ablation Navistar catheter (Biosense Webster Inc.) to the sites where the QRS axis corresponded and was similar to the pace map (Figure 2A). After 25 RF applications, VT cycle length was significantly prolonged to 340 ms and lasted less than 20 seconds by program-
med stimulation reproducibly, therefore the session was ended.

However, the VT recurred a few days after the first RF ablation. The patient then underwent another EPS procedure and RF ablation on the 8th hospital day. During the first EPS procedure, a 4 mm-tip ablation catheter was used. However, insufficient RF energy was delivered to the diseased area due to the significantly thickened myocardium. Therefore, we used an 8 mm-tip ablation catheter for the second EPS session. The VT induced by RV programmed stimulation was the same VT morphology and cycle length as the first session and was sustained. Entrainment mapping could then be performed.

Entrainment mapping was performed around the site where the QRS axis corresponded to the site of the RF application sites in the first session. Entrainment with fusion was observed close to the LV anterior-apical wall. Both isolated pre-potentials (*) and large potentials (△) are recorded by the ablation catheter. An isolated pre-potential (*) preceding the onset of the QRS complex by 42 ms was observed. The post pacing interval is measured to this small potential, which is 337 ms and equal to the VT cycle length. Stimulus-QRSn+1 (arrow) is 379 ms and the Egn+2-QRSn+3 is 379 ms (arrow). The N + 1 difference equals the PPI-TCL difference; both are zero. Measurements using the ABL3-4 Eg as the fiducial point are also shown. The S-Vn+1 is 404 ms, and the Egn+2-Vn+3 is also 404 ms. (see text for discussion)

I, III, aVF, V1: body surface standard leads, RVa: right ventricular apex, ABL1–2: distal pair of electrodes on the ablation catheter, ABL3–4: proximal pair of electrodes on the ablation catheter, PPI: the post pacing interval, S: stimulus, Eg: electrogram
same as the first session (Figure 2B). Although the VT was induced by RV extrastimulation, second session ended because the VT was not sustained and VT cycle length significantly prolonged from 340 to 400 ms and lasted less than 5 seconds. This site was near the border zone which was located between the low and normal voltage areas in the LV anterior-apical wall in CARTO voltage map obtained from the first session.

We felt that it would be difficult to completely eliminate the VT by RF ablation alone. Thus we initiated an administration of 400 mg/day of amiodarone. After that, the VT cycle length did not prolong and terminate spontaneously, giving the appearance of a VT storm, until after the second session of RF ablation and administration of amiodarone.

We recommended the implanted cardioverter defibrillation (ICD) to prevent sudden cardiac death. However, an ICD could not be implanted because the patient refused stubbornly and ventricular fibrillation could not be induced by burst and triple extra pacing protocol.

Finally, no episodes of VT have appeared after the patient left the hospital. Now, the patient remains under close observation as an outpatient and is being treated with 100 mg/day of amiodarone. So far, VT has not recurred for two years.

Discussion

Fabry disease is an inherited X-linked lysosomal storage disease resulting from the deficient activity of the enzyme α-GAL and the accumulation of its glycolipid substrate, globotriaosylceramide (GL-3), particularly in the vascular endothelium. Typical symptoms of this disease are a youth-onset cerebral infarction, LV hypertrophy, renal dysfunction, abdominal pain, angiookeratoma, hypohidrosis and burning pain in the extremities. In particular, exacerbated kidney failure, heart disease or stroke may lead to an early death.

Nowadays, many cases of cardiac sudden death in Fabry disease patients have been reported. ERT with α-GAL, which prevents the accumulation of GL-3, is the only effective treatment for Fabry disease. ERT also prevents further functional deterioration of the diseased organs and improves the impaired function.2–4 It has been recognized that an early diagnosis of Fabry disease may be crucial for the patient’s prognosis.5,6 Since 2004, ERT for Fabry disease has been available in Japan. In this patient, ERT was continued since May of 2004. We encountered a Fabry disease patient with sustained VT. Constant and progressive fusion was confirmed by RV rapid pacing, and the mechanism of VT was considered to be reentry.7 Entrainment mapping was performed in the LV endocardium, but entrainment with concealed fusion could not be observed in any sites of LV endomyocardium. Although pacing was performed from various parts of the endocardium during sinus rhythm, a perfect pace map could not be observed. We could not identify any breakthrough points to the endocardial site. Accordingly, we presumed that the location of the VT reentry circuit exit might be in the myocardium. Figure 3B shows the entrainment mapping just before the VT termination. During entrainment from the ablation catheter, entrainment with QRS fusion was observed. Both isolated pre-potentials and large potentials are recorded by the ablation catheter (Figure 3B). An isolated pre-potential, which preceded the onset of the QRS complex by 42 ms, was recorded at a point, close to the anterior apical wall during VT. Electrical noise introduced during pacing obscured the electrograms at the stimulating ablation catheter electrodes. Comparing the proximal and distal potentials recorded by the ablation catheter suggests that the large potential might also be captured in a localized electrogram. The post pacing interval (PPI) is measured to the local pre-potential, which is 337 msec and equal to the VT cycle length (TCL). Furthermore, the N + 1 difference equaled the PPI-TCL difference and was 0 at re-entry circuit sites in this case.7 This site is consistent with an outer loop. A pre-potential was probably the activation at the outer loop very close to the exit, and the large potential was the activation of the healthier tissue, just outside of the reentry circuit. The ablation catheter was considered to be located just outside of the exit of the reentry circuit (Figure 4).

RF energy, which might have reached the reentry circuit exit in the myocardium, successfully terminated the VT. Generally outer loop sites may be in relatively broad regions of the reentry path, explaining the low incidence of tachycardia termination.8,9 But, if an isolated pre-potential is present at such a site, it increases the likelihood of VT termination.10 In our case, it is probable that the outer loop site with a pre-potential is near a narrower potion of the circuit exit in the myocardium, from which the pre-potential is recorded. However, the RF energy was not sufficient to reach the deepest part of the diseased area. We believed that was the reason why the VT circuit was not completely eliminated.
Patients with Fabry disease, particularly those with cardiac Fabry disease, have a high incidence of cardiac sudden death due to fatal arrhythmias and heart failure.1) To date, only a handful of studies have reported Fabry disease patients associated with sustained VT. Most of them were implanted with ICD, and to the best of our knowledge, no studies have reported a successful RF ablation in those using the CARTO system and entrainment mapping. In the present case, the arrhythmia was not completely cured by RF ablation alone; however, a hybrid therapy with amiodarone along with RF ablation could successfully control the VT. In general, if patients with Fabry disease are not treated with ERT, the cardiac muscle fibers will rapidly degenerate, which may lead to sudden death due to fatal arrhythmias or heart failure. In the present case, it is noteworthy that the VT occurred 4 years after the ERT had been initiated. Although the patient had progressive LV hypertrophy, the LV contraction was maintained and the EPS revealed no ventricular fibrillation. The ERT could have controlled the myocardial degeneration; however, how the ERT affects the reentry mechanism remains unsolved. A cardiac defibrillator should be implanted in order to prevent any sudden cardiac death in such cases, but our patient did not wish to undergo an ICD implantation. The patient needs to be kept under close observation in order to decide whether an ICD is necessary.

References

Figure 4
Schema of the VT reentry circuit. The reentry circuit is indicated with black arrows. An ablation catheter is located close to the reentry circuit exit. Small and large potentials are recorded by the catheter. A small pre potential (•) is the local electrogram which is captured with pacing, and considered to be the outer loop activation very close to the isthmus exit. A large potential (△) is also captured, and considered to be the activation of the healthier tissue outside of the reentry exit.