Histopathological Verification for Successful Ablation of Mitral Isthmus Ventricular Tachycardia Complicated with Cardiac Sarcoidosis

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Abstract

A 68-year-old man died a few days after catheter ablation of drug-resistant, monomorphic ventricular tachycardia (VT) complicated with cardiac sarcoidosis. The diagnosis of mitral isthmus VT was made from electrophysiological observations, including electro-anatomical activation and voltage map, pace-mapping, entrainment mapping and ablation outcome. On autopsy of the heart, sarcoidic lesion with scattered fibrous tissue in the mitral isthmus was non-transmural, and the surviving myocardium serving as the reentry circuit in the endomyocardium was isolated from the adjacent viable epicardium, enabling the sustenance of macroreentry across the mitral isthmus. Non-transmural lesions produced by RF delivery created a barrier sufficient to interrupt the myocardial bundles located in the mitral isthmus, eliminating the mitral isthmus VT.

Key words: Mitral isthmus, ventricular tachycardia, cardiac sarcoidosis, electro-anatomical mapping, entrainment pacing, radiofrequency catheter ablation, human heart histopathology


Introduction

Sarcoidosis is a multisystem granulomatous disease of unknown etiology. Cardiac involvement may occur in as many as more than 50% of patients in Japan (1). Sustained ventricular tachycardia (VT), one of the manifestations of cardiac sarcoidosis, occurs frequently, of which the most common mechanism is presumed to be reentry probably due to the slow conduction caused by myocardial scar tissue (2, 3). Recently, some studies have reported the effectiveness of catheter ablation of VT complicated with cardiac sarcoidosis refractory to medical therapy (4, 5). However, descriptions of histopathologic examinations of the origin of the VT complicated with cardiac sarcoidosis, successfully ablated are limited to case reports (5, 6). Furthermore, although the mitral isthmus is a well-known critical region of slow conduction in some patients presenting with VT after healed myocardial infarction (7-10), there is no report of mitral isthmus VT complicated with cardiac sarcoidosis. We describe a case of mitral isthmus VT complicated with cardiac sarcoidosis, treated with radiofrequency (RF) ablation, followed by autopsy of the heart, and discuss the pathological characteristics of the origin of the VT and their implications for RF ablation.

Case Report

A 68-year-old man was admitted to our hospital for catheter ablation of drug-resistant monomorphic VT. He had no previous history of acute myocardial infarction. He had undergone triple coronary artery bypass graft surgery at the age of 61, for ischemic heart disease without myocardial infarction. The 12-lead electrocardiogram during sinus rhythm showed poor progression of r waves in leads V1 to V₅. A VT with right bundle branch block (BBB) and superior axis...
drugs. Using a CARTO X-P which were uncontrollable with several antiarrhythmic ablation was performed due to frequent episodes of VT

Electrophysiological study and catheter ablation

QRS morphology (VT1), and another with right BBB and inferior axis QRS morphology (VT2) were clinically documented. Left ventriculography showed severe, diffuse hypokinesia and a left ventricular ejection fraction of 28.7%. There was no clinical evidence of extra-cardiac disease.

Electrophysiological study and catheter ablation

Although the patient suffered from pneumonia, catheter ablation was performed due to frequent episodes of VT which were uncontrollable with several antiarrhythmic drugs. Using a CARTO X-P™ electro-anatomical mapping system (Biosense-Webster, Diamond Bar, CA), we identified a 32.3 mm × 26.1 mm low voltage area (defined as bipolar electrograms <0.3 mV) during sinus rhythm at the base of the left ventricular postero-lateral endocardial surface (Fig. 1A). A QRS resembling the morphology of VT1 or VT2 was produced when pacing along the posterior, postero-lateral and lateral wall adjacent to the mitral annulus (Fig. 2), suggesting the presence of a large zone of slow conduction with multiple exits, ranging from the posterior wall to lateral wall, adjacent to the mitral annulus. VT1 and VT2 were both inducible with programmed ventricular stimulation, though only VT1 was sufficiently sustained to allow the recording of an electro-anatomical activation map, which revealed the site of the earliest ventricular activation at the edge of the low voltage area, near the postero-lateral mitral annulus (Fig. 1B). Entrainment pacing during VT1, adjacent to the mitral annulus, where a low-amplitude, early diastolic potential (DP) was detected, was associated with concealed entrainment and a long spike-QRS delay, equal to the DP-QRS interval, and the difference between a post-pacing interval (PPI) of the DP and the tachycardia cycle length was less than 30 ms, suggesting that the mitral isthmus was the critical pathway of the reentrant circuit (Fig. 3). Moreover, entrainment pacing during VT1, approximately 1 cm away from the mitral annulus, was associated

Figure 1. A. Electro-anatomical map of the left ventricle (LV), including voltage map during sinus rhythm. Healthy tissue > 0.6 mV represented by pink color, scar border (0.1-0.6 mV), green/blue, and scar (< 0.1 mV), grey/red. The low voltage zone was 26.1 mm perpendicular to the mitral annulus, 32.2 mm parallel to the mitral annulus and 9.5 mm away from the mitral annulus. Three dotted lines indicate the targeted ablation lines, located along the mitral annulus, parallel and perpendicular to the mitral annulus in the low voltage area. The red tags mark the actual ablation sites. B. Activation map during VT1. Lines 1, 2 and 3 indicate sectional lines corresponding to the sections in Fig. 4A, B and C, respectively. C. Magnified macroscopic view of the injured myocardium. The heart was sectioned along the line between the base of the left atrial appendage and the left ventricular apex. The ablated injured myocardium is located at the base of the postero-lateral left ventricular endocardial surface, between the anterior (APM) and the posterior papillary (PPM) muscles, which are smooth and slightly discolored, probably from the ablation procedure. LA: left atrium. D. Section of LV free wall near the aneurysm showing ghosts of multinucleate giant cells with the infiltration of inflammatory mononucleocytes. Hematoxylin and Eosin staining.
Figure 2. A. Twelve-lead electrocardiogram recorded during VT1. B. Twelve-lead electrocardiogram recorded during VT2. C-F. Pace map recorded along the mitral annulus at 6:00, 4:30, 3:30 and 3:00 o’clock. A spike-QRS delay, indicated as numbers on each panel, was measured at each pacing site. The dotted line marks the onset of the QRS complex. Note that the QRS morphology of VT1 resembled that of the pace map at 6:00, 4:30 and 3:30 o’clock, while the QRS morphology of VT2 resembled that of the pace map at 3:00 o’clock.

Figure 3. Surface electrocardiogram and intracardiac electrograms during ventricular entrainment pacing and concealed entrainment, with an S-S interval of 370 ms from the ablation catheter (ABL) adjacent to the mitral annulus (A), and right (B) and left (C) oblique fluoroscopic views, showing the position of the catheters. Low-amplitude, diastolic potentials (arrowheads) were detected from ABL 1-2, 343 ms before the onset of QRS complex. The last pacing stimulus captures the next QRS (marked by an asterisk) with a 366 ms spike-QRS delay, similar to the 355 ms DP-QRS interval. The difference between 418 ms post-pacing interval of the early diastolic potential and the tachycardia cycle length of 397 ms was less than 30 ms, suggesting that the tip of ABL was located near the entrance of the zone of slow conduction of the reentry circuit. I, II, V1 and V5 = 12-lead surface electrograms, HRA: high right atrium, RVA: right ventricular apex, RVOT: right ventricular outflow tract.
with constant fusion, with a PPI nearly equal to the tachycardia cycle length, consistent with an outer loop of the reentrant circuit. Using an 8F Thermocool™, irrigated tip ablation catheter ( Biosense-Webster ), a 45-second RF application at a maximum power of 30 W and maximum temperature of 43° delivered at the mitral annulus, terminated VT1, 17 seconds after the onset of RF delivery. A total of 18 additional linear and crosswise RF applications, representing a total of 25,457 J, were delivered along the mitral annulus in the low voltage area (Fig. 1A), eliminating the inducibility of VT1 and VT2.

The patient, however, died of sepsis resulting from drug-resistant, severe pneumonia, which was not associated with the ablation procedure, 16 days after the ablation procedure, and a post mortem examination of the heart was performed.

**Post mortem examination**

The heart was autopsied and fixed in 10% formalin within 5 hours of death. The weight of the heart was 520 g. The left ventricle was dissected along the lateral wall to expose the ablation region (Fig. 1C). Visual inspection revealed no left ventricular dilatation and the presence of a 4.0×2.5 cm lateral aneurysm, with a smooth and whitish endocardial surface (Fig. 1C). The aneurysm was sectioned transmurally (Fig. 1B), perpendicular to the mitral annulus, and divided into anterior (Fig. 4A and B), mid (Fig. 4C and D) and posterior (Fig. 4E and F) myocardial blocks, which were stained with Masson trichrome, and processed for standard microscopic analyses.

Microscopic examination of LV free wall near the aneurysm revealed ghosts of multinucleated giant cells with the infiltration of inflammatory leukocytes, consistent with the lesion of cardiac sarcoidosis (Fig. 1D). By light microscopy, the sarcoidic lesion with scattered fibrous tissue was mostly confined within 2/3 of the endomyocardium, though it reached the epicardium in some areas (Fig. 4D, E and F), not consistent with an ischemic injury. Likewise, the sarcoidic lesion immediately below the mitral annulus corresponding to the successful ablation site was non-transmural, where neither multinucleate giant cells nor inflammatory leukocytes were observed. The electro-anatomical area of low voltage corresponded with the sarcoidic lesion. Since complete revascularization with coronary artery bypass graft surgery had been performed for ischemic heart disease with-

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**Figure 4.** Macroscopic views of the ablated, injured myocardium sectioned anteriorly (A), laterally (B) and posteriorly (C), perpendicular to the mitral annulus. D-F: Light microscopic views corresponding to the sections shown in A, B and C. A: The thickness of the aneurysmal wall measured 8 mm. The thickness of the submitral myocardium measured 10 mm. Two dark discolored hemorrhagic spots were observed within the subendocardial layer of the aneurysm (arrows). B: This section includes the posterior papillary muscle and tendon. The thickness of the aneurysmal wall measured 6 mm. The thickness of the submitral myocardium measured 10 mm. Dark, discolored continuous, hemorrhagic lesions were observed within the subendocardium, between the submitral annulus and the base of the papillary muscle. C: The thickness of the submitral myocardium measured 7 mm. Three hemorrhagic spots were observed immediately below the mitral annulus, in the central portion of the aneurysm and near the attachment of the posterior papillary muscle, respectively. See text for descriptions of panels D-F.
out healed myocardial infarction, non-aneurysmal LV lesion exhibiting severe hypokinesia might also be caused by sarcoid lesion. The region of ablation was visible as 3, discontinuous linear hemorrhagic endocardial areas inside the aneurysm, including 1) a line along the mitral annulus, 2) a parallel line approximately 1 cm away from the mitral annulus, and 3) a line perpendicular to the mitral annulus. The ablated area measured 25×20 mm on the endocardial surface and it was approximately 4 mm deep, except in the center of the aneurysm, where the lesion was transmural.

Discussion

In the present case, the diagnosis of mitral isthmus VT was based on the electrophysiological observations made in the area of the sarcoid lesion, between the mitral annulus and the left postero-lateral aneurysm (mitral isthmus), including electro-anatomical activation and voltage map, pace-mapping, entrainment mapping and ablation outcome (7-10).

Although the pathological substrate of VT complicating a healed MI has been well characterized (6, 11), the human pathology of mitral isthmus responsible for VT in a patient with non-ischemic cardiomyopathy remains limited. Matsuyama et al reported the presence of isolated myocardial bundles running along the annulus, which might have been the arrhythmogenic substrate, in a patient with mitral isthmus VT associated with idiopathic dilated cardiomyopathy (12). Scanavacca et al described the presence of tissue surviving between the infero-lateral scar of the left ventricle and the mitral annulus, in a patient presenting with mitral isthmus VT associated with Chagas’ disease (13). In the present case, it is noteworthy that the sarcoidic lesion in the mitral isthmus was characterized by transmural lesions and surviving myocardium in the scar, confined to the subendocardium. The surviving myocardium, acting as the reentrant substrate in the endomyocardium, was probably isolated from the adjacent viable epimyocardium, enabling the sustenance of macroreentry across the mitral isthmus. Thus, the non-transmural lesions produced by RF ablation were sufficient to interrupt the myocardial bundles located inside the mitral isthmus, eliminating the mitral isthmus VT.

The authors state that they have no Conflict of Interest (COI).

References


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