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CASE REPORT
Heart Failure

Life-threatening ventricular arrhythmia and left ventricular dysfunction associated with anti-mitochondrial antibody-positive myositis: a case report

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Background Anti-mitochondrial antibody (AMA)-positive myositis is an atypical inflammatory myopathy characterized by chronic progression of muscle atrophy and cardiac involvement. Few detailed reports have shown the clinical course of the cardiac complications of AMA-positive myositis.

Case summary A 47-year-old man presented with shortness of breath on exertion. Cardiac dilatation was visible on chest X-ray, and echocardiography demonstrated diffuse hypokinesis with a reduced left ventricular (LV) ejection fraction of 30%. He had mild muscle weakness in the bilateral iliopsoas muscles, and his creatine kinase (CK) and anti-mitochondrial M2 antibody levels were elevated. A liver biopsy showed no findings of primary biliary cholangitis. Coronary angiography revealed normal coronary arteries. An endomyocardial biopsy showed interstitial fibrosis and marked degeneration of the mitochondria. Fluorodeoxyglucose (FDG)-positron emission tomography/computed tomography showed circumferential abnormal accumulation in the LV myocardium, and he was diagnosed with cardiomyopathy associated with AMA-positive myositis. Optimal drug therapy for heart failure was started, and a cardiac resynchronization therapy-defibrillator was implanted. However, his cardiac function did not improve, and he was hospitalized due to ventricular tachycardia storm 5 years after the diagnosis. Ventricular tachycardia was terminated by radiofrequency catheter ablation on the LV-anterior papillary muscle. Steroid therapy was initiated and resulted in a decreased uptake of FDG and a normalized CK level at 3 months after his second discharge; however, LV systolic dysfunction remained 1 year later.

Discussion Anti-mitochondrial antibody-positive myositis can affect the myocardium and cause severe LV dysfunction and life-threatening ventricular arrhythmia over time.

Keywords Anti-mitochondrial antibody-positive myositis • Endomyocardial biopsy • Ventricular tachycardia • Left ventricular dysfunction • Case report • Magnetic resonance imaging • Near-infrared spectroscopy-intravascular ultrasound

ESC Curriculum 6.2 Heart failure with reduced ejection fraction • 6.5 Cardiomyopathy • 5.6 Ventricular arrhythmia

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Learning points

- Anti-mitochondrial antibody-positive myositis can present with latent inflammatory myopathy characterized by chronic progression of muscle atrophy and cardiac involvement.
- Anti-mitochondrial antibody-associated cardiomyopathy can cause severe left ventricular dysfunction and life-threatening ventricular arrhythmia.
- In cases of unexplained cardiomyopathy, we should perform systemic screening.

Introduction

Anti-mitochondrial M2 antibodies are autoantibodies related to primary biliary cholangitis (PBC) that are associated with myositis. Anti-mitochondrial antibody (AMA)-positive myositis is reported to be a latent inflammatory myopathy characterized by skeletal muscle atrophy, chronic progression of respiratory muscle disorders, and cardiac complications.[1,2] Supraventricular arrhythmias are frequently reported in patients with AMA-positive myositis[3]; however, the detailed clinical course of cardiac complications remains unclear.

We report the case of a patient with AMA-positive myositis who presented with left ventricular (LV) dysfunction and developed sustained ventricular tachycardia (VT).

Timeline

Date	Event
June 2012	Catheter ablation for atrial flutter Echocardiogram: left ventricular ejection fraction (LVEF) 55%
November 2013	Pacemaker implantation due to sinus arrest with dizziness Echocardiogram: LVEF 45%
May 2014–July 2014	Hospitalized due to heart failure. • Echocardiogram: LVEF 30% • Mild muscle weakness in the bilateral iliopsoas muscles • Elevated creatine kinase (CK), and anti-mitochondrial M2 antibody titres. • Liver biopsy: no findings of primary biliary cholangitis. • Endomyocardial biopsy: interstitial fibrosis and degeneration of mitochondria • Fluorodeoxyglucose (FDG)-positron emission tomography computed tomography: circumferential abnormal accumulation in the left ventricular (LV) myocardium. • Diagnosed as cardiomyopathy associated with anti-mitochondrial antibody-positive myositis.
July 2014	• Optimal drug therapy for heart failure initiation and a cardiac resynchronization therapy-defibrillator implantation
June 2018	Development of atrial fibrillation Routine echocardiogram: LVEF 35%
April 2019	Hospitalized due to ventricular tachycardia storm • Successful catheter ablation on LV-anterior papillary muscle • Initiation of prednisolone (40 mg/day)
July 2019	Decreased FDG uptake and normalized CK level
April 2020	Routine echocardiogram: LVEF 30%

Case presentation

A 47-year-old man presented with shortness of breath on exertion and was admitted to our institution in April 2014. He had undergone catheter ablation for atrial flutter 2 years previously. He also had undergone DDD-pacemaker implantation 6 months previously because 24-h Holter monitoring detected sinus arrest with dizziness. Electrocardiography prior to pacemaker implantation showed first-degree atrioventricular block, left-axis deviation, and poor R-wave progression in leads V1–4 (*Figure 1*).

On admission, his blood pressure was 108/72 mmHg, and his heart rate was 70 b.p.m. with dual-chamber pacing. Electrocardiography showed atrial and ventricular pacemaker spikes, and chest X-ray revealed cardiac dilatation. Echocardiography demonstrated diffuse hypokinesis with a reduced LVEF of 30% and an enlarged LV end-diastolic diameter (58 mm). Blood tests revealed increased brain natriuretic peptide, 91.1 pg/mL; creatine kinase (CK), 1342 IU/L; CK-MB, 32 IU/L; and increased troponin T, 0.082 ng/mL. Manual muscle testing revealed mild muscle weakness (Grade 4 of 5) in the bilateral iliopsoas muscles; however, his needle electromyography findings were normal. Of note, anti-mitochondrial M2 antibodies were detected (titre: 28.6 IU/L; reference range <7.0 IU/mL). His aspartate transaminase level was elevated at 58 U/L; however, his alanine transaminase and bilirubin levels were normal. Liver biopsy showed no findings of PBC. Coronary angiography showed no significant stenosis. Right ventricular endomyocardial biopsy revealed interstitial

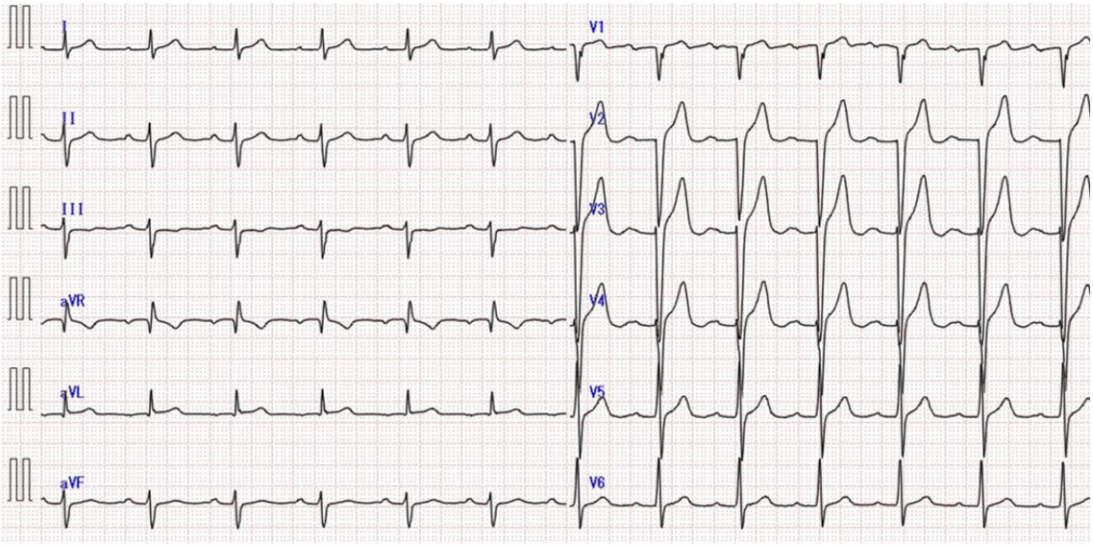


Figure 1 An electrocardiogram prior to pacemaker implantation showed first-degree atrioventricular block, left-axis deviation, and poor R-wave progression in leads V1–4.

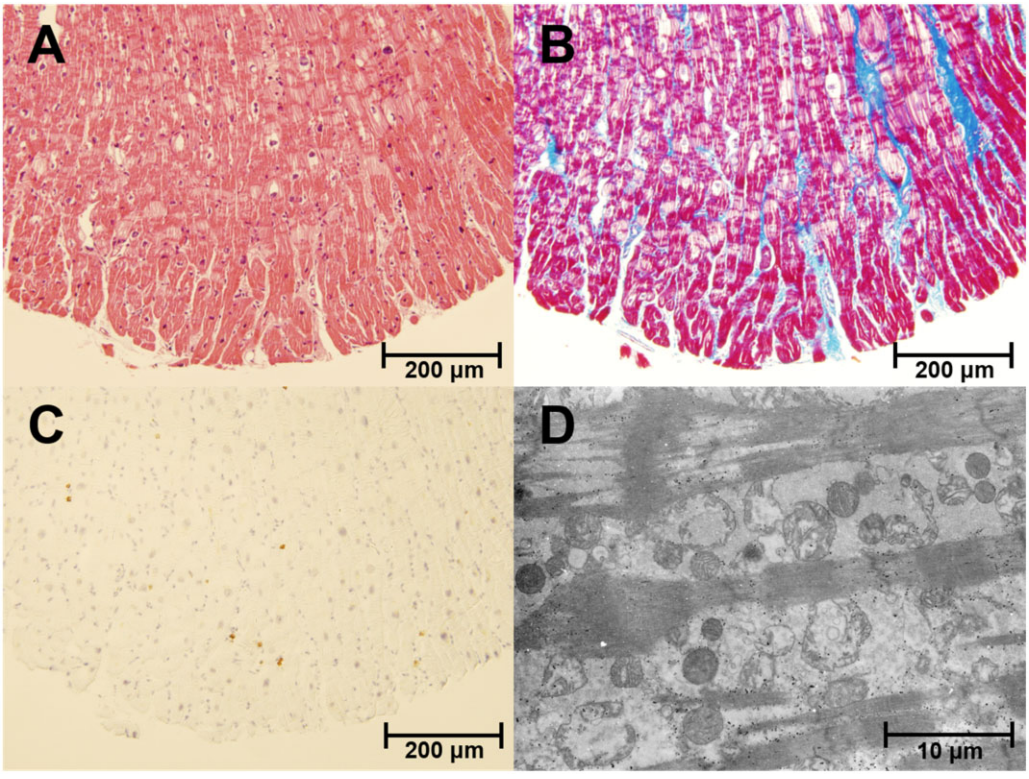


Figure 2 (*A*, *B*) An endomyocardial biopsy from the right ventricle revealed cardiomyocyte hypertrophy with interstitial fibrosis. (*C*) Mild infiltration of CD3-positive T cells was observed. (*D*) Electron microscopy showed marked degeneration of the mitochondria.

fibrosis with sparse CD3-positive T cells (*Figure 2A–C*). Electron microscopy revealed marked mitochondrial degeneration (*Figure 2D*). Fluorodeoxyglucose positron emission tomography (FDG-PET)/computed tomography (CT) showed abnormal circumferential accumulation of FDG in the LV myocardium, including the papillary muscles (*Figure 3*). There was no FDG accumulation in the lymph

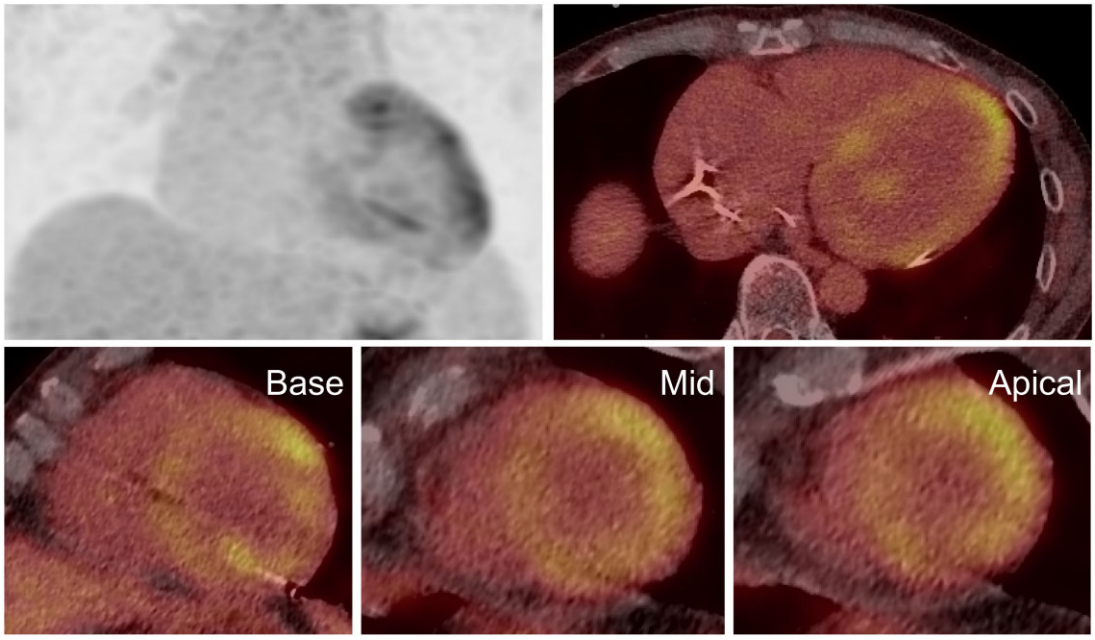


Figure 3 Fluorodeoxyglucose positron emission tomography/computed tomography revealed the abnormal circumferential accumulation of fluorodeoxyglucose in the left ventricular myocardium.

nodes. Accordingly, we diagnosed the patient with cardiomyopathy associated with AMA-positive myositis. Steroid therapy was proposed; however, the patient declined it. Optimal medical therapy for LV dysfunction was initiated with a beta-blocker, an angiotensin-converting enzyme inhibitor, and an aldosterone antagonist. A cardiac resynchronization therapy-defibrillator (CRT-D) was implanted due to concerns about the deterioration of the cardiac function due to the coexistence of a reduced LVEF and frequent right ventricular pacing.

Thereafter, the patient's CK, CK-MB, and troponin T levels remained high, and the LVEF did not improve. In June 2018, bradycardic atrial fibrillation developed and became chronic. Oral anticoagulant therapy was initiated, but catheter ablation was not performed for rhythm control because the left atrial enlargement was significant. In April 2019, he was hospitalized due to frequent VT. Drug therapy including amiodarone, sotalol, and mexiletine failed to control VT, and catheter ablation was performed. A CARTO-3 system (Biosense Webster Inc., Diamond Bar, CA, USA) and intracardiac echocardiogram (CartoSound; Biosense Webster) were used concomitantly for mapping. Some delayed potentials were identified at the LV-anterior papillary muscle (APM). Clinical VT was easily induced (*Figure 4A*). Entrainment mapping during VT was performed at the LV-APM, where the catheter recorded diastolic potentials, and revealed concealed fusion, suggesting that this site was located in the critical isthmus of VT (*Figure 4B* and *C*). Clinical VT was successfully terminated by radiofrequency catheter ablation at this point. We performed FDG-PET/CT, and the abnormal accumulation in the entire circumference of the left ventricle, including the APM, was confirmed to be enhanced in comparison to that at the diagnosis of AMA-positive myositis five years previously (*Figure 5A*). He agreed to the initiation of steroid therapy with prednisolone (40 mg/day). After 3 months, the FDG accumulation had decreased (*Figure 5B*), and his CK, CK-MB, and troponin T levels normalized; however, his LVEF remained low at 1 year after the initiation of steroid therapy. No recurrence of VT has been observed during follow-up.

Discussion

In 2012, Maeda *et al.*[1] reported that 11.3% of 212 consecutive patients with myositis were positive for AMA, and the AMA-positive myositis group showed cardiac complications (e.g. arrhythmia and heart failure) more frequently (8 of 24 patients) than the AMA-negative myositis group. Albayda *et al.*[2] reported that five of seven patients with AMA-positive myositis exhibited cardiac complications. Few case reports have described AMA-positive myositis and cardiac complications[4–7]; however, the relationship between AMA and cardiac dysfunction has not been fully elucidated. Matsumoto *et al.*[8] reported interstitial fibrosis with the infiltration of CD3-positive T cells in the ventricular myocardium of a patient with AMA-M2-related cardiomyopathy. Saito *et al.*[9] performed immunostaining for pyruvate dehydrogenase complex E2 subunit (PDC-E2), an antigen for anti-mitochondrial M2 antibodies, and showed granular staining in the cytoplasm of all cardiomyocytes. They also showed degenerated mitochondria in cardiac myocytes by electron microscopy and reported that PDC-E2 was released into the cytoplasm due to mitochondrial damage, suggesting that inflammatory activation against these damaged cells could result in myocarditis. In our case of AMA-positive myositis, endomyocardial biopsy revealed interstitial fibrosis, marked degeneration of the mitochondria, and the existence of

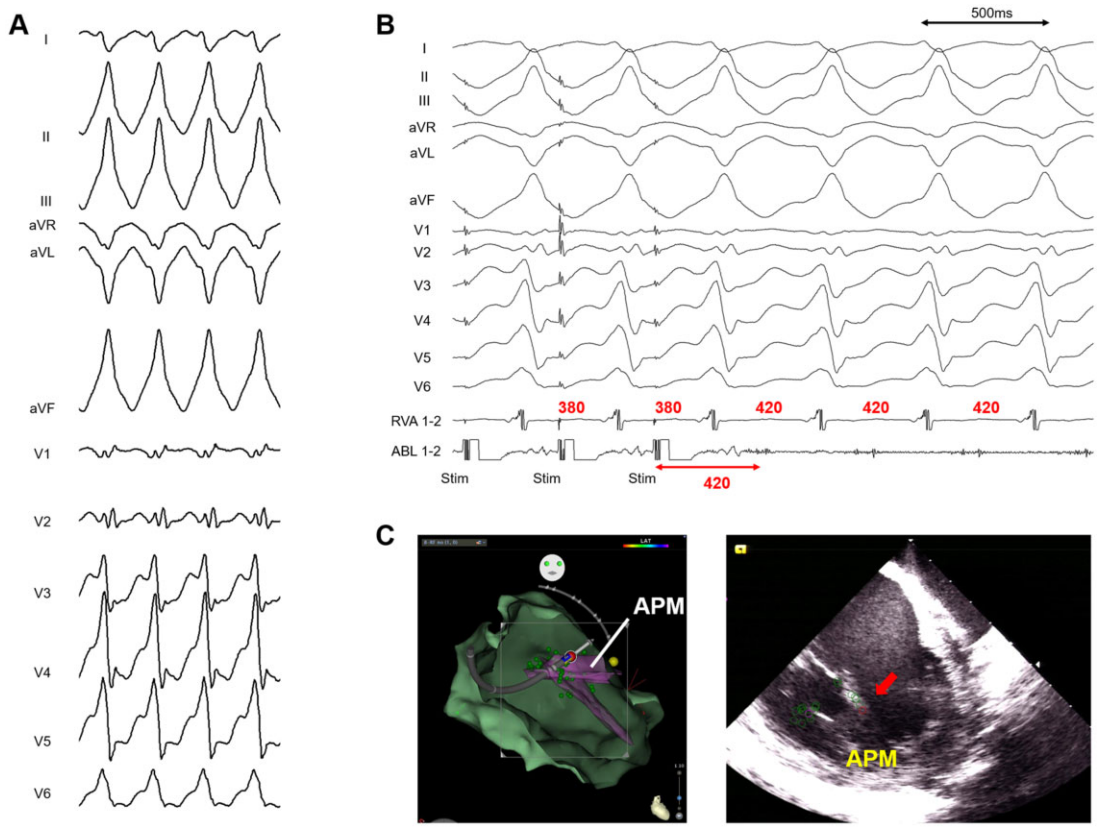


Figure 4 The electrophysiological study and catheter ablation for ventricular tachycardia. (*A*) Twelve-lead electrocardiograms showing clinical ventricular tachycardia with a cycle length of 400 ms (*B*) Entrainment with concealed fusion during sustained clinical ventricular tachycardia at the site of successful ablation. The morphology of the QRS complex during pacing (left side) was identical to the ventricular tachycardia morphology (right side). The post-pacing interval was equal to the tachycardia cycle length. (*C*) The site of concealed entrainment was confirmed by three-dimensional reconstruction of the left ventricle and the anterior papillary muscle (left panel) and real-time CartoSound® intracardiac echocardiographic imaging (right panel). Red circles and red arrows indicate the location of the catheter tip. APM, anterior papillary muscle.

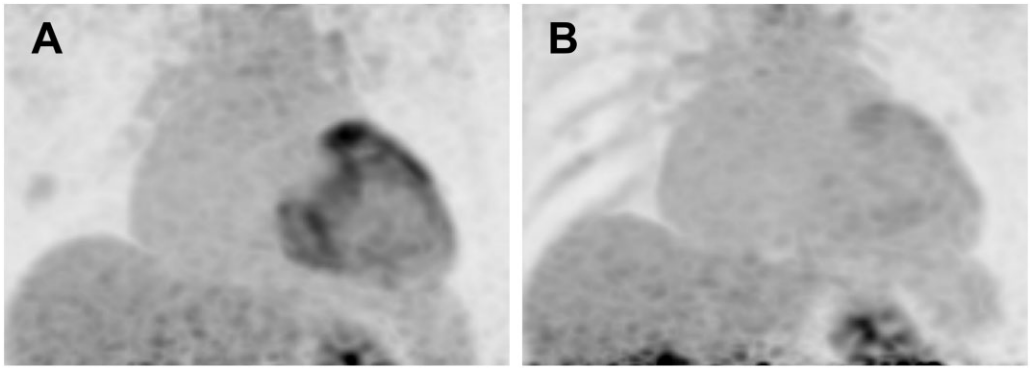


Figure 5 (*A*) The fluorodeoxyglucose uptake in the ventricular myocardium was enhanced compared with that at the diagnosis of anti-mitochondrial antibody-positive myositis 5 years previously. (*B*) The fluorodeoxyglucose uptake had decreased by 3 months after the initiation of prednisolone.

CD3-positive T cells, which are consistent with the findings of AMA-associated myocardial disorder.

In our patient, PET-CT was useful for diagnosing the localization of inflammation and assessing disease activity. Cardiac magnetic resonance imaging may also be useful in myocarditis screening.[7]

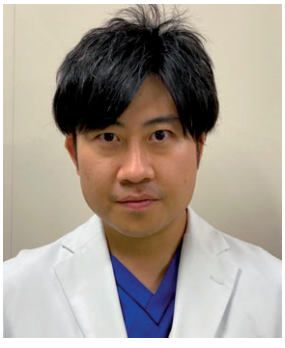
Few studies have reported the detailed mechanisms of VT in patients with AMA-positive myositis. Our patient had re-entrant VT and arrhythmogenesis in the LV-APM. The abnormal accumulation of FDG in the LV-APM might suggest that AMA-related myocardial damage was involved in the arrhythmogenesis. The presence of inflammation may have been associated with antiarrhythmic-drug-refractory VT. The origin of VT was presumptive, as the VT morphology was similar to previous reports of ablation on the LV-APM.[10]

The effectiveness of immunosuppressive therapy for cardiomyopathy complicated by AMA-positive myositis remains to be clarified. In two Japanese case reports describing the administration of steroids before the progression of LV dysfunction, the CK and troponin T levels improved within 3 months.[7,8] Our patient presented with active myocardial inflammation and was therefore treated with steroids, but his cardiac function did not improve. The patient's 5-year-long period of inflammation was therefore considered to have caused the onset of replacement fibrosis, which is refractory to steroid therapy. In addition, conventional therapies for heart failure may not be effective without early immunosuppressive therapy.

For patients with heart failure and a reduced LVEF, angiotensin–neprilysin inhibition and SGLT2 inhibitor treatment have been shown to reduce the risks of death and hospitalization for heart failure.[11,12] Since these drugs have recently been approved in Japan, we are considering their use.

To our knowledge, this is the first report to show the detailed clinical course of the cardiac complications of AMA-positive myositis including a period of up to 5 years without steroid therapy. In our case, while PBC was not diagnosed and the symptom of muscle weakness was mild, cardiac complications were prominent. We should keep in mind that AMA antibody-related myopathy can cause severe LV dysfunction and life-threatening ventricular arrhythmia over time.

Lead author biography



Yuki Hasegawa obtained his medical degree in 2010 at Niigata University and has been a member of the medical staff at Niigata University Medical & Dental Hospital from 2015. He has specialized in clinical electrophysiology. He is interested in revealing the mechanism of ventricular fibrillation.

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Supplementary material

Supplementary material is available at *European Heart Journal—Case Reports* online.

Slide sets: A fully edited slide set detailing these cases and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

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