Premature ventricular contraction-induced dilated cardiomyopathy: a case report

Jonathan Sen* and John Amerena

Cardiology Research Unit, University Hospital Geelong, Barwon Health, PO Box 281, Geelong, Victoria 3220, Australia

Background	Premature ventricular complexes (PVCs) are ectopic heartbeats caused by early myocardial depolarizations, previously thought to be benign. Recent studies found high PVC burden above 24% can induce or contribute to cardiomyopathy and heart failure. We present a case of PVC-induced dilated cardiomyopathy (DCM).
Case summary	A 68-year-old woman was admitted with pneumonia after an overseas trip with a preceding viral respiratory tract infection. An initial chest X-ray was suggestive of cardiomegaly. A transthoracic echocardiogram (TTE) revealed DCM with global systolic dysfunction (left ventricular ejection fraction <30%) without valvular lesions. Biochemistry and coronary angiography were normal. Clinical deterioration occurred despite medical therapy. A 24-h Holter monitoring detected 27% PVCs, which was thought to have caused DCM. As an alternative to cardiac resynchronization therapy and an implantable cardiac defibrillator for primary prevention, ablation of the PVC focus led to complete suppression of ectopy. Post-procedure TTEs and Holter monitoring showed normalized systolic function and low PVC burden.
Discussion	Because high PVC burden can lead to cardiomyopathy and heart failure, suppression of PVC should be considered to restore ventricular function for patients with structural heart disease and frequent symptomatic PVCs. This case highlights that PVCs may be a modifiable risk factor for heart failure that can be successfully treated with pharmacological therapies or catheter ablation.
Keywords	Cardiomyopathy • Case report • Catheter ablation • Dilated cardiomyopathy • Heart failure • Premature ventricular complexes

Learning points

- High premature ventricular contraction burden appear to be independently associated with left ventricular dysfunction, ventricular dyssynchrony, and subsequent heart failure.
- Ventricular ectopic ablation may be useful treatment to suppress premature ventricular contraction and restore ventricular function for patients with structural heart disease and frequent symptomatic premature ventricular contractions.

Introduction

Premature ventricular complexes (PVCs) are ectopic heartbeats caused by early depolarizations of the ventricular myocardium instead of the sinoatrial node.[1] Premature ventricular complexes are present in about 4% of the general population on 12-lead electrocardiography (ECG) and 40–75% of patients on 24–48 h Holter monitoring.[2] Although previously thought to be benign, observational studies in recent years have associated PVCs with increased cardiac mortality and hospitalizations.[2–4] Premature ventricular complex burdens above 24% can induce or contribute to cardiomyopathy and heart failure.[5,6]

* Corresponding author. Tel: +3 4215 0000, Email: research@jonathansen.com

Dilated cardiomyopathy (DCM) is characterized by reduced left ventricular ejection fraction (LVEF) below 45%, or fractional shortening below 25%, DCM is the third most common cause of heart failure and the main indication for cardiac transplantation.[7] High PVC burden is now recognized as a potential cause of DCM,[8] and may be associated with myocarditis, enhanced ventricular myocardial automaticity, and genetic cardiomyopathies (such as mutations in titin, desmoplakin, and filamin C genes).[2]

Premature ventricular complexes originating from the epicardium and right ventricular outflow tract (RVOT) with broad QRS complexes leading to mechanical ventricular dyssynchrony are particularly associated with cardiomyopathy.[6] Patients with frequent PVCs can be considered for catheter ablation if there is persistent symptomatic left ventricular (LV) dysfunction refractory to medical management in DCM and where frequent PVCs preclude biventricular pacing.[6] Ablation may improve cardiac ejection fraction and outcomes in PVC-induced cardiomyopathy, however, long-term follow-up data are limited.[9]

Timeline

Case presentation

A 68-year-old woman was admitted 2 weeks after returning from Bali, Indonesia, with symptoms of pneumonia including dyspnoea on minimal exertion, chest pain, and a productive cough. This was preceded by viral upper respiratory tract symptoms (e.g. coryza and sore throat) experienced during her holiday. She did not report smoking, alcohol, or recreational drug use. She had no family history of cardiomyopathy, heart failure, or sudden cardiac death. HIV screening was not performed. On admission, her respiratory rate was 20 breaths per minute with an oxygen saturation of 98% on room air. Her blood pressure was 140/70 mmHg, and her jugular venous pressure was not elevated. On auscultation, she had dual heart sounds with no murmurs. However, there were crepitations and reduced breath sounds bibasally.

An admission ECG confirmed sinus rhythm, a heart rate of 64 b.p.m., with frequent monomorphic PVCs, which were asymptomatic. Normally conducted complexes were low-voltage but did not exhibit any abnormal waveforms. Her initial chest X-ray was suggestive

May 2015	Recovered from viral respiratory infection in Bali, Indonesia
	Diagnosed with pneumonia 2 weeks post-return to Geelong, Australia
	Posterioranterior projection of chest X-ray suggestive of cardiomegaly
	CT pulmonary angiogram with right lower lobe consolidation and bilateral pleural effusions with adjacent bibasal atelectasis.
August 2015	*TTE* demonstrated dilated cardiomyopathy with severely impaired LVEF 30%, LVEDD of 7.1 cm (normal <5.6 cm), moderate diastolic dysfunction, and no valvular pathology[a]
October 2015	NYHA I functional class
	Started on bisoprolol 1.25 mg daily and perindopril 2.5 mg daily[b]
December 2015	NYHA II functional class
	Signs and symptoms of fluid overload, required diuresis with furosemide
	Changed to nebivolol 1.25 mg on alternate days due to intolerance
	Changed perindopril to candesartan due to dry cough
February 2016	*Holter monitor* showing sinus rhythm with fusion complexes, average heart rate of 74 b.p.m., PVC burden: 27 522/101 027 beats (27%) ventricular ectopic beats. Thousand seven hundred and twenty-nine couplets, 9065 bigeminal cycles, 154 runs (monomorphic/non-sustained VT), and longest lasting 5 beats.
	Coronary angiogram with mild diffuse irregularities in the mid-to-distal LAD; LVDP 20 mmHg
	TTE with LVEF 25–28%, LVEDD of 6.2 cm; dilated left ventricle with severe left ventricular systolic dysfunction, mild-moderate MR
	Furosemide changed to spironolactone 25 mg daily
May 2016	*TTE* with LVEF 32%, LVEDD of 6.5 cm, and mild-moderate MR
June 2016	PVC ablation to anterolateral left ventricular papillary muscle
July 2016	*TTE* with LVEF 46% and LVEDD of 6.3 cm
February 2017	*Holter monitor* with sinus rhythm, minimal PVCs 2324/96 510 beats (2.4%) ventricular ectopic beats, 21 couples, and 0 runs.
	TTE with LVEF 51%, LVEDD of 5.5 cm, and mild left atrial dilation
August 2017	NYHA I functional class
	TTE with LVEF 61%, LVEDD of 4.9 cm, trace MR, and normal left atrial size
February 2018	NYHA I functional class
	TTE with LVEF 64%, LVEDD of 5.4 cm, borderline left ventricular hypertrophy, and normal systolic function

Blue: changes to medications and red: intervention.

LAD, left anterior descending artery; LVDP, left ventricular developed pressure; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; NYHA, New York Heart Association functional classification; PVC, premature ventricular contraction; TTE, transthoracic echocardiogram; VT, ventricular tachycardia.

[a]The confirmatory TTE was done as an outpatient after discharge from hospital. Unfortunately, the waiting time for a public TTE at the time was 3 months.

[b]The general practitioner was asked to follow-up the TTE result and referred to cardiology, as appropriate. The waitlist for an outpatient cardiology review resulted in the patient being seen ~2 months after the TTE result.
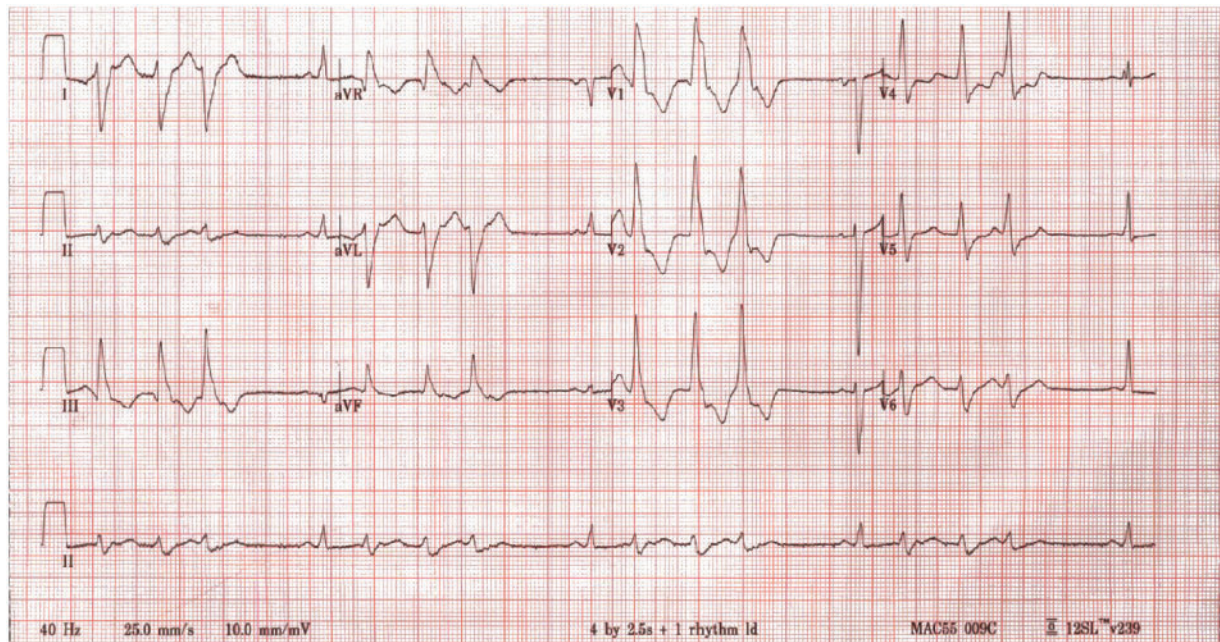
Figure I Electrocardiogram suggested that the premature ventricular complexes originated from anterior papillary muscle.

of cardiomegaly and a high-sensitivity troponin I was negative. A computed tomography pulmonary angiogram revealed right lower lobe consolidation with bilateral pleural effusions. There was no pulmonary embolism or pericardial effusion.

Her pneumonia was treated with moxifloxacin 400 mg orally daily due to previous anaphylaxis to penicillins. The baseline corrected QT interval (QTc) was 490 ms with no significant increase after starting moxifloxacin. She completed a 7 day course of moxifloxacin after discharge and did not require diuresis given her euvolaemic state.

Outpatient investigations included biochemistry for endocrine, autoimmune, rheumatological, and infiltrative causes, all of which were unremarkable. A transthoracic echocardiogram (TTE) revealed DCM with global systolic dysfunction (LVEF <30%) and mildly reduced right ventricular systolic function without valvular pathology or congenital cardiac abnormalities.

At 4 months post-discharge, she was minimally symptomatic [New York Heart Association (NYHA) functional classification I], was able to walk 4–6 blocks on an incline, and did not have orthopnoea, paroxysmal nocturnal dyspnoea, or peripheral oedema. However, due to systolic dysfunction on her TTE, she was started on guideline-based medical therapy (GBMT) in the form of daily perindopril 2.5 mg and bisoprolol 1.25 mg. Bisoprolol was switched to nebivolol 1.25 mg on alternate days due to intolerance manifesting as fatigue and myalgia. Further, perindopril was changed to candesartan 4 mg daily due to a dry cough. These were the maximal tolerated final doses prior to ablation. Despite GBMT, her condition progressed to NYHA Class II symptoms within 7 months of diagnosis, with a rapid reduction in her exercise tolerance to only 1–2 blocks on level ground. Furosemide was initiated for fluid overload and changed to spironolactone 25 mg daily 5 weeks later.

A 24-h Holter monitor detected a significant PVC burden of 27% (27 522/101 027 beats) with 154 runs of non-sustained ventricular tachycardia (longest run of 5 beats). The PVCs mainly comprised monomorphic ventricular bigeminy and, to a lesser degree, couplets. Coronary angiography was normal. Cardiac magnetic resonance imaging is only funded for selected indications in Australia, and is not widely available; it was not performed in this case, as she did not fulfil the criteria for Medicare subsidy.

Given the above results, it was thought plausible that the patient had developed PVC-induced DCM. ECG morphology suggested an anterior papillary muscle origin for the PVCs (*Figure 1*). Upon retrospective review of the patient's medical records (12-lead ECGs), frequent PVCs preceded the admission with pneumonia by 2 years, thus reinforcing PVCs as a potential causative aetiology of the DCM.

Serial TTEs at 6 and 9 months since the initial TTE demonstrated progressive deterioration in cardiac function (Supplementary material online, *Video S1*). With tolerated medical therapy, the ectopic frequency was reduced, but incompletely suppressed.

As an alternative to cardiac resynchronization therapy and implantable cardiac defibrillator for primary prevention, the decision was made to attempt ablation targeting the PVC origin. An electrophysiology study was performed, which confirmed the PVC origin seen on surface ECG. This was then combined with intra-cardiac echocardiography (together, termed 'electroanatomical mapping') to ensure accuracy of delivered radiofrequency ablation. Real-time imaging allowed active visualization and verification of target sites and ablation probe positioning. After localizing the origin through pacing and activation mapping, targeted ablation of the region was successfully performed (*Figure 2*), which led to complete suppression of ectopy.
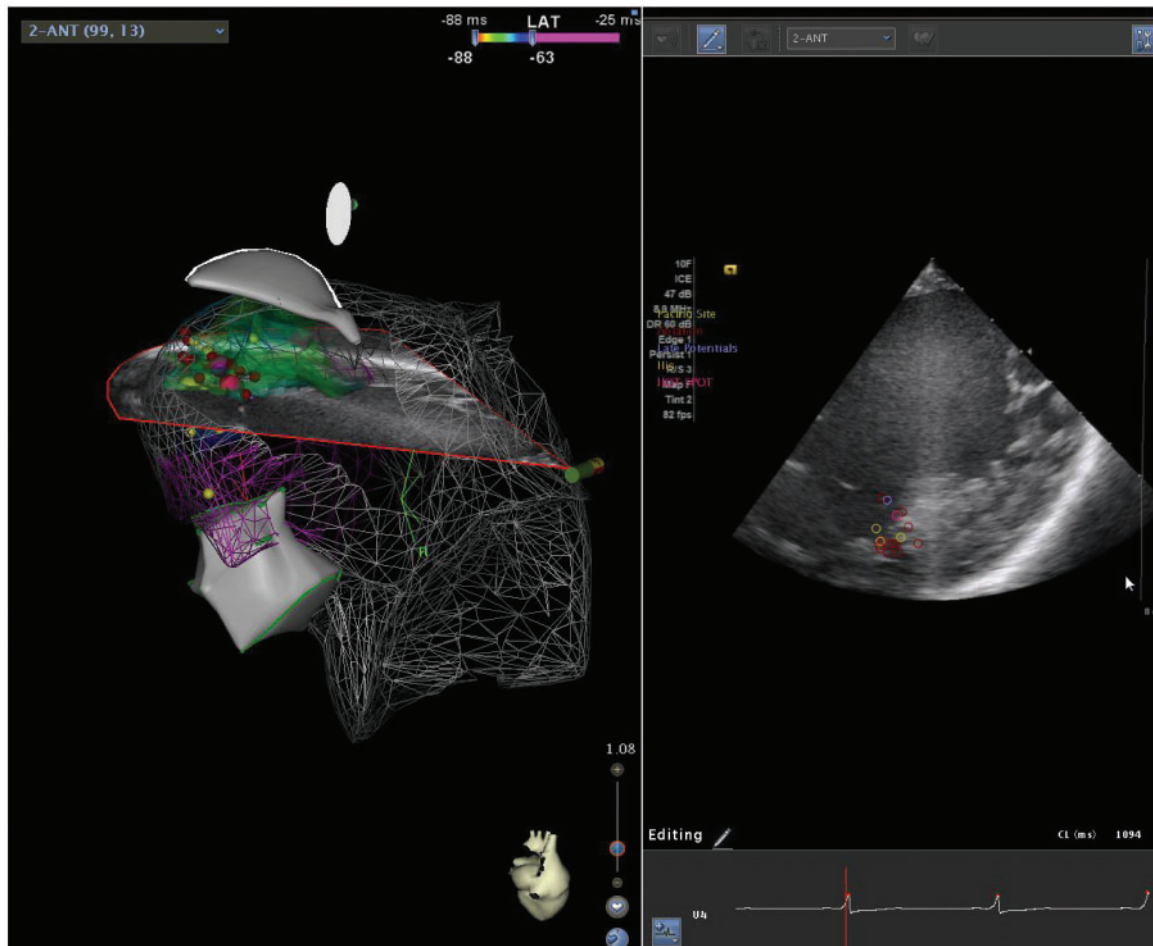
Figure 2 CARTO 3—sound map. Left panel: three-dimensional wireframe representation of the ventricle. Solid grey structure at bottom of three-dimensional model: posteromedial papillary muscle; Green highlighted area: anterolateral papillary muscle. Right panel: Live two-dimensional intra-cardiac ultrasound image. Its projection and orientation in three-dimensional space can be seen in the left panel (red outlined 'fan'). Both panels: red circle: ablation site; yellow circle: pacing site during EP study; and blue circle: late potentials.

Post-procedure echocardiograms (Supplementary material online, *Video S2*) and 24-h Holter monitoring (*Figure 3*) demonstrated return to normal systolic function and considerably reduced PVC burden to 2.6% (2324/96 510 beats) without non-sustained ventricular tachycardia. There was no pre-excitation on serial ECGs. Maintenance therapy with beta-blockade has been uptitrated to 1.25 mg daily nebivolol and will be continued indefinitely. The remainder of her medications remained unchanged, maintaining her heart rate and blood pressure at nominal levels (64 b.p.m. and 120/84 mmHg). Twenty months post-ablation, the patient reports profound improvement in cardiac function which has enabled a return to her baseline level of function and quality of life.

Discussion

The concept of PVC-induced DCM has been proposed in recent years.[2] The minimum PVC burden thought to result in cardiomyopathy is 10%, however, PVC burdens greater than 24% appear to be independently associated with LV dysfunction, ventricular dyssynchrony, and heart failure.[10] Premature ventricular complexes may be a modifiable risk factor for heart failure that can be successfully treated with pharmacological therapies or catheter ablation. Based on absent elevation of cardiac troponin results in this case, myocarditis is thought an unlikely cause of LV dysfunction. While troponin cannot definitively exclude myocarditis,[11] the patient's marked response to targeted ablation would be inconsistent with myocarditis being the underlying cause of PVCs. For the same reason, we feel HIV to be unlikely.[12]

Reversal of PVC-induced DCM has been shown to improve systolic function and mortality, as well as prevent hospitalization and progression to heart failure.[5] One of the strengths of the approach in this case was extended follow-up confirming improvement in cardiac function 20 months post-ablation.

Another strength of this study is the use of optimal GBMT prior to invasive procedures.[13] Beta-blockers are first-line therapy in management of ventricular arrhythmia and prevention of sudden cardiac
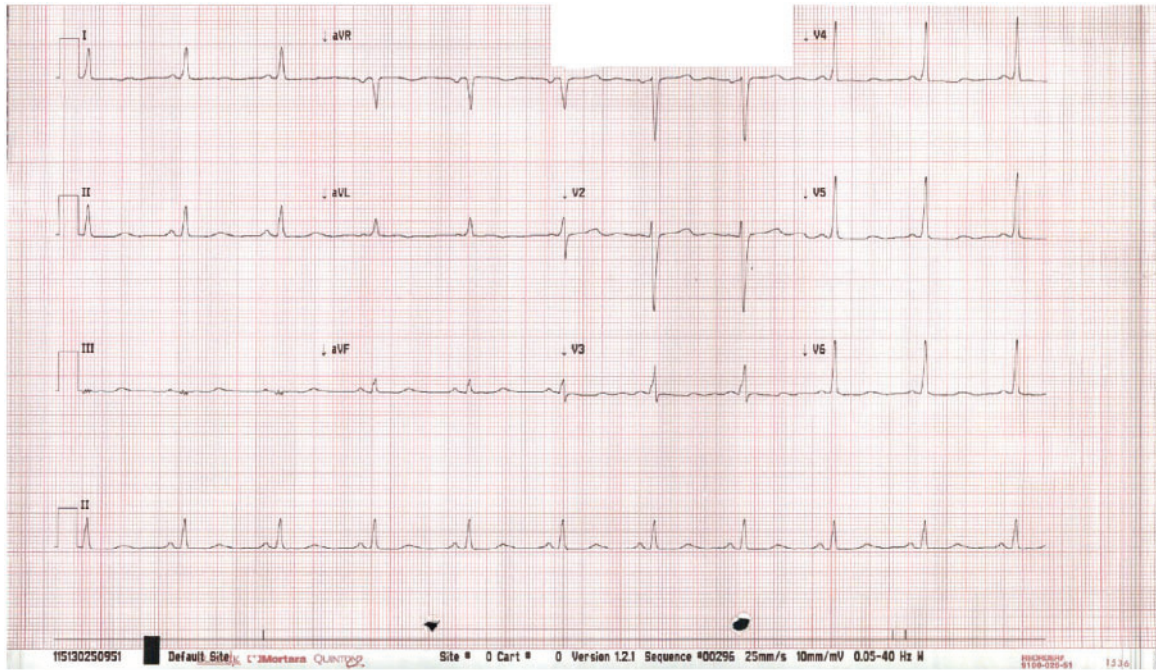
Figure 3 Electrocardiogram post-ablation.

death in accordance with European Society of Cardiology (ESC) guidelines. Bisoprolol is a cardio-selective beta-blocker with long half-life allowing for once daily dosing and has been found to suppress PVCs through competitive beta-adrenoreceptor inhibition.[13] In this case, bisoprolol was substituted with nebivolol which may be better tolerated as it is among the most cardio-selective for beta-1-receptors.[14]

According to the 2015 ESC guidelines for management of patients with ventricular arrhythmias, ablation should be considered to suppress PVC and restore ventricular function for patients with structural heart disease and frequent symptomatic PVCs (Class IIA recommendation).[13]

While PVCs commonly originate from the RVOT and typically demonstrate a left bundle branch block (LBBB) pattern in lead V1, the ECG in this patient suggested that the PVCs originated from an anterior papillary muscle, which manifested as a right bundle branch block (RBBB) pattern in lead V1. Furthermore, if the frontal plane axis is leftward deviated, it would likely reflect posteromedial papillary muscle/left posterior fascicle, while a right axis deviation would likely reflect anterolateral papillary muscle/left anterior fascicle.[15] It is important to note the technical barriers with respect to ablation. Depending on the origin of the PVCs, myocardial thickness and cardiac anatomical variation may impede adequate electrical isolation, requiring alternative management strategies.

Conclusion

In this case, high PVC burden from a single papillary muscle origin resulted in DCM, which was treated successfully with targeted ablation, resulting in improved long-term health outcomes 20 months post-procedure.

Supplementary material

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

Slide sets: A fully edited slide set detailing this case 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 image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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