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CASE REPORT
Heart failure

Stellate ganglion blockade combined with nifekalant for patients with electrical storm: a case report

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Background Although both stellate ganglion blockade and nifekalant are effective treatment options for electrical storm, the clinical effect of their combination is uncertain.

Case summary A 71-year-old male patient was admitted to our hospital with acute myocardial infarction and heart failure. Emergency coronary angiography revealed triple-vessel disease. Although coronary artery bypass grafting was planned, the patient experienced electrical storm before the surgery could be performed. Despite complete revascularization by percutaneous coronary intervention, mechanical circulatory support and administration of antiarrhythmic agents (amiodarone and lidocaine), electrical storm was not controlled. After stellate ganglion blockade was initiated on the 9th day of hospitalization, ventricular arrhythmia decreased. However, when stellate ganglion blockade was temporarily discontinued, ventricular arrhythmia increased substantially. Subsequently, combination therapy with stellate ganglion blockade and nifekalant was initiated, after which ventricular arrhythmia disappeared completely. Afterwards, the patient had no further ventricular arrhythmia episodes, and his haemodynamic status gradually improved. The patient was discharged from hospital in an ambulatory condition and did not experience arrhythmia during the follow-up.

Discussion This case demonstrates that combination therapy with stellate ganglion blockade and nifekalant can completely suppress ventricular arrhythmia, suggesting that blocking multiple conduction pathways is a key to treating refractory electrical storm.

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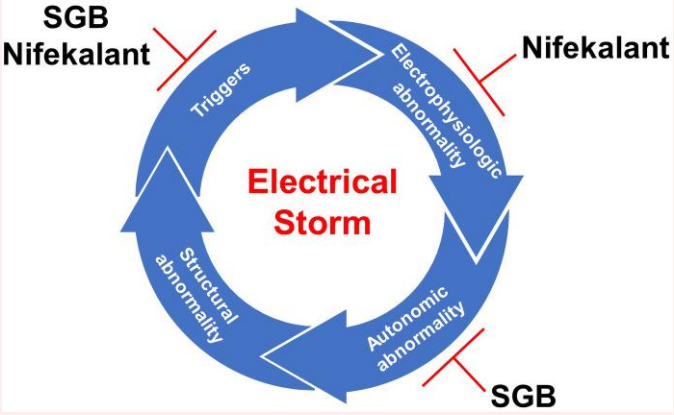
Graphical Abstract



Potential mechanism of the combination of stellate ganglion blockade and nifekalant for suppressing electrical storm. The occurrence and persistence of electrical storm were potentially associated with a vicious cycle. SGB and nifekalant blocked this cycle from multiple angles. SGB, stellate ganglion blockade.

Keywords Case report • Electrical storm • Ventricular arrhythmia • Nifekalant • Stellate ganglion blockade • Combination therapy

ESC curriculum 5.6 Ventricular arrhythmia • 6.4 Acute heart failure • 7.1 Haemodynamic instability • 3.2 Acute coronary syndrome

Learning points

- Although both stellate ganglion blockade (SGB) and nifekalant have been reported to be effective for electrical storm (ES), the clinical effectiveness of their combination is unclear.
- This case report shows that combining SBG and nifekalant may be a valuable approach for ES resistant to traditional treatments.

Introduction

An electrical storm (ES) is a critical condition with significant mortality and morbidity,[1,2] and its appropriate management is crucial. The efficacy and safety of stellate ganglion blockade (SGB) have been reported recently in patients with ES.[3–5] Additionally, nifekalant, a pure potassium channel blocker, is effective in patients with ES refractory to other antiarrhythmic drugs.[6,7] However, few studies have evaluated the efficacy of combining SGB and nifekalant in patients with ES. Here, we present a case of refractory ES, where ventricular arrhythmia was remarkably suppressed via concomitant SGB and nifekalant administration.

Timeline

Time	Event
On admission	The patient was hospitalized because of acute myocardial infarction with heart failure. Emergency coronary angiography (CAG) showed triple-vessel disease and coronary artery bypass grafting (CABG).
4 h after performing CAG	While waiting for CABG, the patient developed ventricular tachycardia (VT) and ventricular fibrillation (VF).
1 h after the occurrence of VT/VF	Emergency percutaneous coronary intervention (PCI) was performed to the left coronary artery, and veno-arterial extracorporeal membrane oxygenation (VA-ECMO) was inserted. Despite initiating amiodarone and lidocaine, VT and VF recurred.
Day 2	PCI was performed on the right coronary artery.
Day 5	VA-ECMO and IABP were changed to Impella 5.0.
Day 9	Left stellate ganglion blockade (SGB) was initiated. VT and VF decreased but did not resolve completely.
day 10	Impella 5.0 was downgraded to IABP.
Day 12	SGB was temporally discontinued. VT and VF increase dramatically.
Day 14	SGB was resumed, and nifekalant was initiated. VT and VF disappeared completely.

Continued

Time	Event
Day 19	IABP was explanted.
Day 23	The patient was transferred to the general ward.
Day 30	Nifekalant was changed to bepridil.
Day 143	A transvenous implantable cardioverter-defibrillator was placed.
Day 164	The patient was transferred to another hospital for rehabilitation.
Day 234	The patient was discharged ambulatory.

Case presentation

A 71-year-old Japanese male patient with a 50-year history of smoking and diabetes without medications presented to our hospital with a 2-day history of dyspnoea. His vital signs were as follows: blood pressure, 124/90 mmHg; heart rate, 104 bpm; respiratory rate, 28 breaths/min; and oxygen saturation, 97% on a 2-L nasal cannula. Physical examination revealed moist rales in both lungs and oedema in the lower extremities. Electrocardiogram revealed ST-segment elevation in the anterior leads with long QT (QTc, 472 msec) (*Figure 1*). A chest radiography demonstrated cardiomegaly with pulmonary congestion. Transthoracic echocardiography revealed a reduced left ventricular ejection fraction (LVEF) of 20% with severe hypokinesis of the anterior wall. Laboratory analysis showed elevated levels of cardiac enzymes [creatine kinase-MB, 70 U/L (normal range, 7–15 U/L); troponin-I, 148, 155 pg/mL (normal range: ≤ 26 pg/mL)]; creatinine [1.24 mg/dL (normal range: 0.65–1.07 mg/dL)]; brain natriuretic peptide [2079 pg/mL (normal range: ≤18.4 pg/mL)] and glycated haemoglobin [8.2% (normal range: 4.9–6.0%)]. No electrolyte abnormalities were observed. Based on these findings, the patient was diagnosed with ST-segment elevation myocardial infarction with congestive heart failure. Subsequently, emergency coronary angiography was performed, revealing three-vessel disease, with severe stenosis of the left anterior descending artery (LAD), left circumflex artery (LCX) and total occlusion of the right coronary artery (RCA) (*Figure 2A–C*). Rentrop Grade 2 collaterals were observed from the septal branch and LCX to the distal portion of the RCA (*Figure 2B*). After a discussion within the cardiology team, including cardiologists, cardiovascular surgeons, cardiovascular nurses and biomedical equipment technicians, we decided to perform coronary artery bypass grafting (CABG) after intra-aortic balloon pump (IABP) implantation. However, the patient experienced ventricular tachycardia (VT) and ventricular fibrillation (VF) before CABG. Despite cardioversion, amiodarone administration (50 mg/h) and general sedation, ventricular arrhythmia recurred, leading to ES. Subsequently, veno-arterial extracorporeal membrane oxygenation (VA-ECMO) was added to IABP to maintain haemodynamics, and percutaneous coronary intervention was performed to improve the coronary flow. Although drug-eluting stents were implanted in the proximal segment of the LAD and LCX (*Figure 2D*), VT/

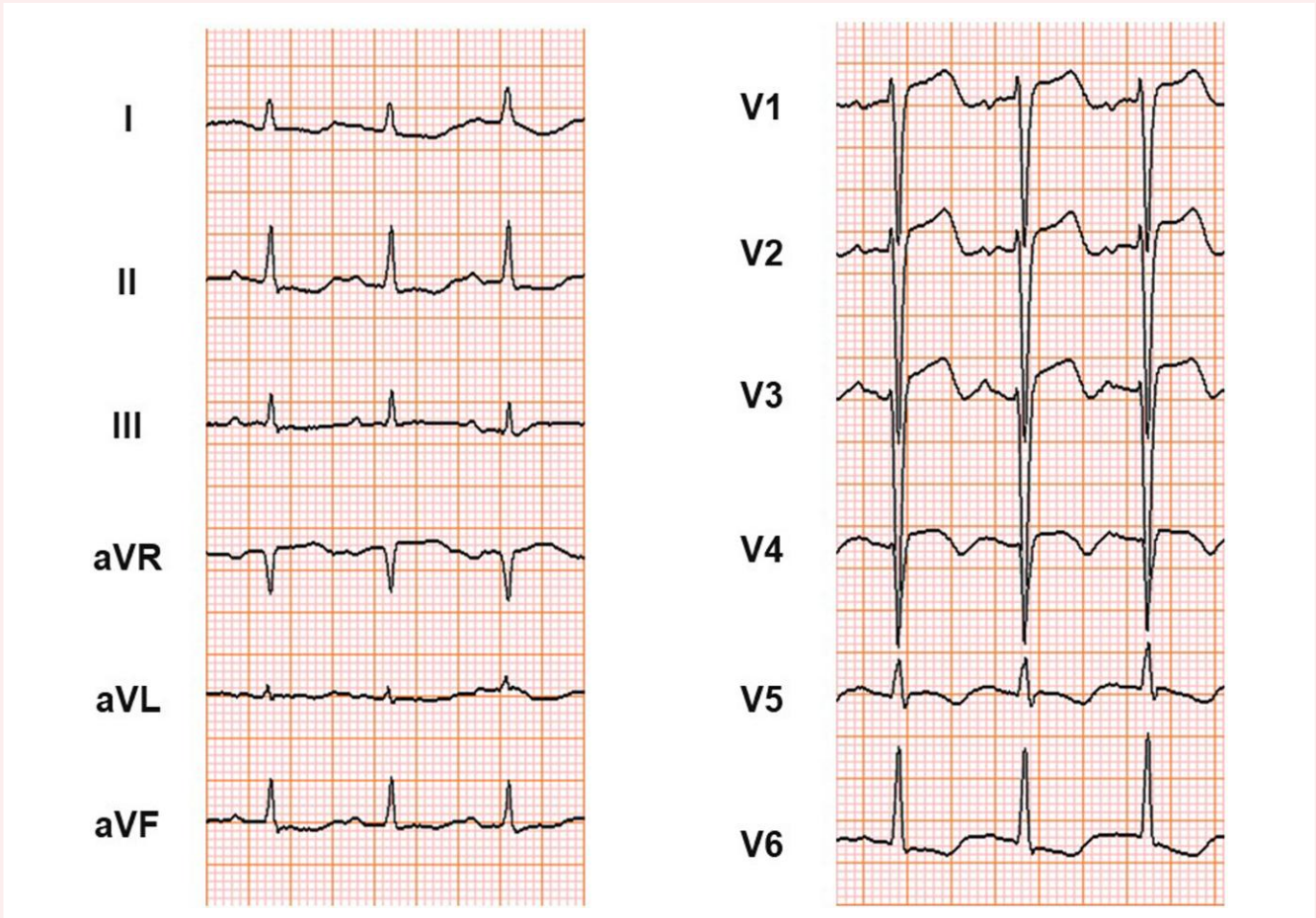


Figure 1 Electrocardiographic findings on admission. Sinus tachycardia (heart rate, 106 bpm) with ST elevation and depression in the anterior leads and the lateral and inferior leads, respectively. QT prolongation was also documented (472 msec).

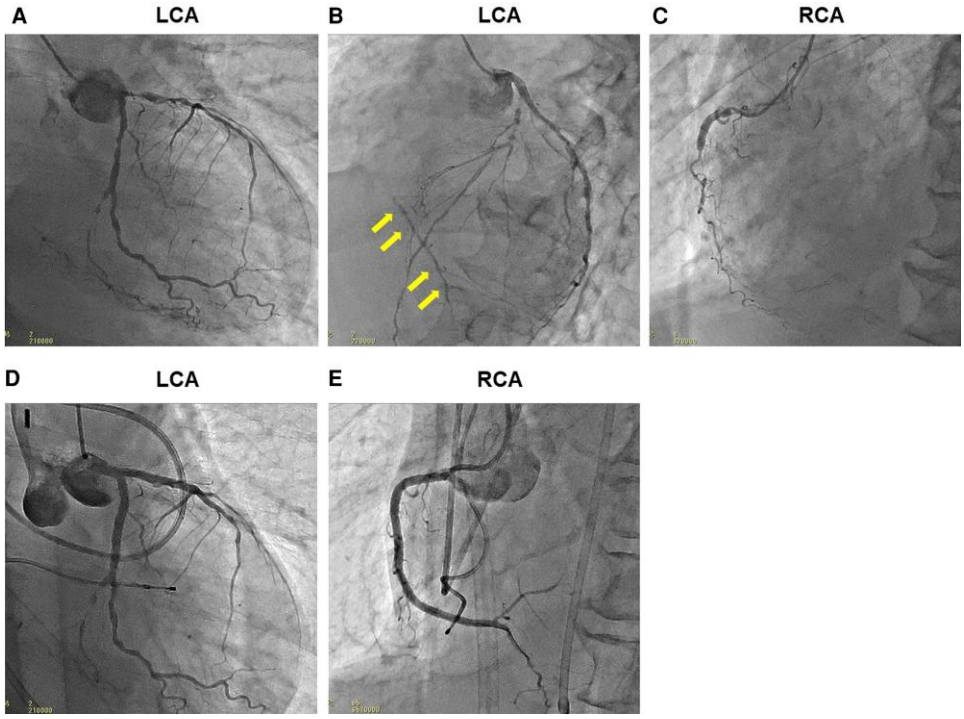


Figure 2 Coronary angiography on admission and after percutaneous coronary intervention. Severe stenosis of the left anterior descending artery, left circumflex artery (*A*, *B*) and total occlusion of the right coronary artery (*C*) with collaterals from the septal branch and left circumflex artery to the distal portion of the right coronary artery (arrows). Drug-eluting stents were implanted in the proximal portion of the left anterior descending artery, left circumflex artery (*D*) and proximal to the distal portion of the right coronary artery (*E*). LCA, left coronary artery; RCA, right coronary artery.

VFs did not decrease; therefore, RCA was also re-vascularized the following day (*Figure 2E*). After complete coronary revascularization, ventricular arrhythmia prevalence decreased; however, VT/VFs occurred easily due to the R-on-T phenomenon associated with QT prolongation (*Figure 3*). Although intravenous lidocaine (80 mg/h) was administered, it did not provide many benefits. After discussions with a clinical cardiac electrophysiologist, catheter ablation was thought to pose a high risk because of unstable haemodynamic status and the absence of a suitable access route. Due to uncontrollable VT/VF recurrence and poor cardiac function improvement, VA-ECMO and IABP were changed to Impella 5.0® (Abiomed Inc., Danvers, MA, USA) on hospitalization Day 5, after which the patient's haemodynamic status stabilized; however, VT/VFs did not completely disappear, and frequent cardioversion was still required. We decided to administer percutaneous left SGB (levobupivacaine, 25 mg twice daily) on the 9th day of admission. Subsequently, the prevalence of VT/VFs requiring cardioversion relatively decreased (but did not disappear completely), and we could de-escalate Impella to IABP. Temporarily discontinuing SGB 5 days after initiation due to the absence of the practitioner who performed the procedure caused a noticeable increase in VT/VFs. Therefore, SGB was considered effective for VT/VF inhibition and was resumed. Subsequently, amiodarone/lidocaine was replaced with nifekalant (20 mg/h). After initiating concomitant SGB and nifekalant, the VT/VFs suddenly disappeared, and no recurrence was observed during the rest of the patient's hospital stay (*Figure 4*). Subsequently, haemodynamic status became stable, and IABP was explanted during hospitalization Day 19. On the 30th day post-admission, nifekalant was switched with 100 mg bepridil, after which QT time did not prolong further, and recurrent VT/VFs were not observed. Next, medication modification and rehabilitation were performed, and the patient was implanted with a transvenous cardioverter-defibrillator. Cardiac resynchronization therapy was not selected because of the narrow QRS duration of 92 msec. Subsequently, the patient was transferred to another hospital for further rehabilitation on hospitalization Day 164. At discharge, his laboratory data showed reduced brain natriuretic peptide and creatinine levels to 495.1 pg/mL and 0.90 mg/dL, respectively, and LVEF was improved to 35%. The patient was prescribed bisoprolol 2.5 mg, enalapril 1.25 mg, spironolactone 25 mg, azosemide 30 mg, empagliflozin 10 mg, and bepridil 100 mg. He was discharged in an ambulatory condition 10 weeks after the transfer and did not experience arrhythmia or heart failure during the 1-month follow-up period.

Discussion

Sympathetic nervous activity is significantly associated with ventricular arrhythmias;[8] therefore, it is logical to assume that SGB will effectively manage this. A clinical study involving 20 patients with ES or incessant VT/VF that appeared refractory to conventional treatment showed that SGB was associated with decreased ventricular arrhythmias and defibrillation.[5] Another retrospective study including 30 patients with ES refractory to standard therapy revealed that 60% experienced ES resolution within 24 h of SGB.[4] Although these sudies depicted SGB as a useful option for managing ES, the evidence level has been insufficient because of the limited sample size.

Nifekalant is a non-selective potassium channel blocker that does not affect the Na channel or β receptors; therefore, it is preferable for managing haemodynamics in cardiac patients. Previous reports have shown that nifekalant might be more useful for ventricular arrhythmia than lidocaine or amiodarone, commonly used to prevent VT/VF recurrence. Nifekalant is reportedly superior to lidocaine regarding the 24 h survival rates in patients

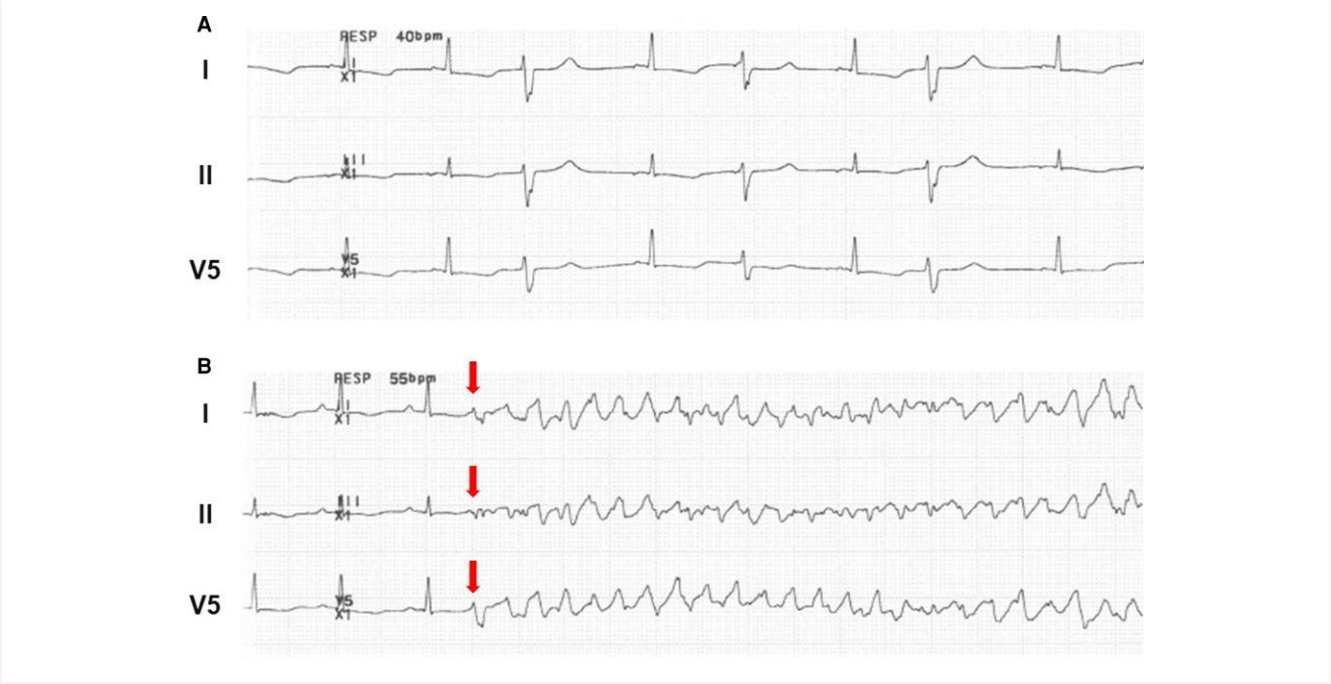


Figure 3 Initiation of ventricular arrhythmia. QT prolongation and frequent premature ventricular contractions were documented immediately before electrical storm occurred (*A*). Electrical storm occurred due to R-on-T phenomenon (arrows) (*B*).

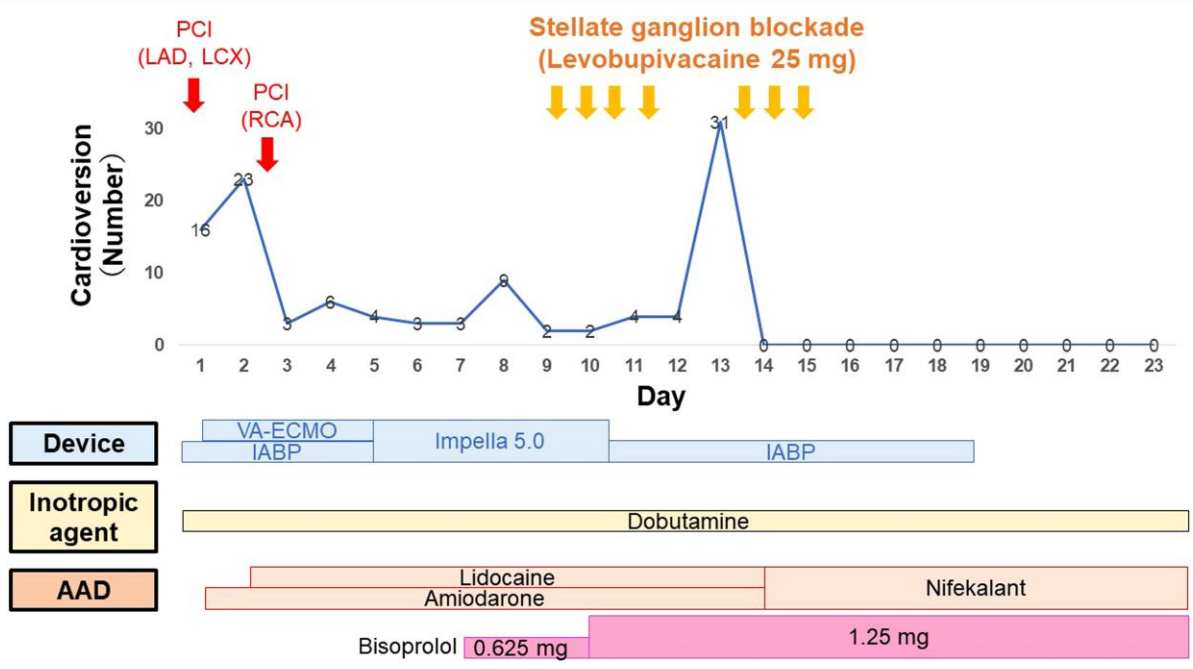


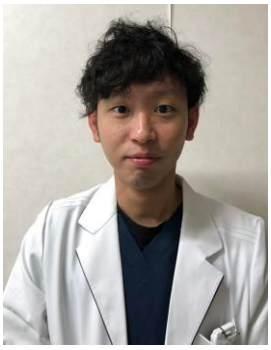
Figure 4 Clinical course of the patient. After revascularization, the number of cardioversions decreased, but ventricular arrhythmia did not disappear. Stellate ganglion blockade was initiated on the 9th day of hospitalization. On discontinuing SGB, ventricular arrhythmia rapidly increased. Combined therapy with stellate ganglion blockade and nifekalant completely suppressed ventricular arrhythmia. AAD, antiarrhythmic drug; IABP, intra-aortic balloon pumping; LAD, left anterior descending artery; LCX, left circumflex artery; PCI, percutaneous coronary intervention; RCA, right coronary artery; VA-ECMO, veno-arterial extracorporeal membrane oxygenation.

with cardiac arrest precipitated by shock-refractory VF.[9] Additionally, it was significantly associated with short- and long-term mortality in patients with shock-resistant VF or pulseless VT, whereas amiodarone was not.[10]

Although SGB and nifekalant have been separately used for ventricular arrhythmias, their combination efficacy is yet to be elucidated. To date, only a small study has addressed this topic.[11] Amino et al. categorized 15 out-of-hospital patients with cardiopulmonary arrest and nifekalant-resistant VT/VFs into two groups based on whether SGB was added ($n = 11$) or not ($n = 4$) to the treatment plan. In the SGB group, seven patients achieved sinus rhythm restoration through cardioversion, whereas all patients in the non-SGB group died of ventricular arrhythmia.[11] Although this study suggested the potential efficacy of concomitant SGB and nifekalant, it excluded statistical analysis to support the significance of this finding because of insufficient sample size. Moreover, the study patients' clinical course was uncertain. Our report is the first to show the efficacy of combining SGB with nifekalant for managing treatment-resistant ES (including mechanical circulatory support) in a patient with severe heart failure. Although the mechanism underlying the efficacy of this combination is not fully understood, a possible explanation is the simultaneous blockade of multiple conduction pathways in the heart. Therefore, breaking this vicious cycle of arrhythmia is essential to completely suppress ES (*Graphical Abstract*). We believe that the combination therapy described in this report is a promising treatment option for refractory ES.

Here, we switched nifekalant to bepridil in the chronic phase. However, we used bepridil for several reasons. First, we did not select oral amiodarone because intravenous amiodarone was ineffective in suppressing ventricular arrhythmia in the acute phase. Next, we expected the effect of the 'multiple channel blockade' of bepridil since we believe it was an important key for decreasing ventricular arrhythmia. Indeed, bepridil is useful for suppressing ventricular arrhythmia in patients refractory to multiple antiarrhythmic drugs.[12] A report also suggested that combining beta-blocker and bepridil did not prolong QTc and QT intervals, whereas bepridil alone prolonged them.[13] Therefore, we thought that bepridil would be effective against ventricular arrhythmia and could be safely used with beta-blockers. Here, we carefully checked electrocardiogram to observe QTc and ventricular arrhythmia recurrence. However, QTc did not prolong further, and no ventricular arrhythmia was observed.

Lead author biography



Takuya Kiyohara received his medical license at Osaka Medical and Pharmaceutical University and is currently working as a cardiologist at Itami City Hospital in Japan. His main area of interest is arrhythmia. He loves his parents.

Supplementary material

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

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 the submission and publication of this case report, including images and associated text, was obtained from the patient in line with the COPE guidelines.

Conflict of interest: None declared.

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Data availability: The data underlying this article cannot be shared publicly due to the privacy of the patient.

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