Case study

Anesthetic Management with Remimazolam in an Arrhythmogenic Right Ventricular Cardiomyopathy Patient with a History of Stable Sustained Ventricular Tachycardia: A Case Report

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ABSTRACT

Aims: Arrhythmogenic right ventricular cardiomyopathy (ARVC) may cause sudden and unexpected deaths in the perioperative period. This study reports a case of ARVC, safely managed using total intravenous anesthesia with remimazolam.
Presentation of Case: A 51-year-old male patient (weight: 100.1 kg, height: 171.0 cm), with a history of ARVC and frequent episodes of stable sustained ventricular tachycardia (VT), underwent open cholecystectomy. The patient underwent total intravenous anesthesia with remimazolam, remifentanil, and a modified thoracoabdominal nerves block perichondrial approach for postoperative analgesia. Hemodynamic stability was maintained throughout the surgery. Catecholamine use was not warranted during the perioperative period. No episodes of stable sustained VT or other cardiovascular episodes were observed.
Discussion and Conclusion: ARVC is a genetically-determined heart muscle disease characterized by life-threatening ventricular arrhythmias in apparently healthy young people. Anesthesiologists should pay close attention to the anesthetic management of patients with ARVC. Remimazolam can be safely used in such cases.

Keywords: arrhythmogenic right ventricular cardiomyopathy, ventricular tachycardia, perioperative sudden cardiac death

1. INTRODUCTION

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a rare but serious cardiovascular disease that can lead to heart failure, potentially fatal ventricular arrhythmias, and perioperative sudden cardiac death (PSCD) [1, 2]. ARVC is an inherited heart disease with a prevalence of approximately 1:5000 [3]. The average age of onset of ARVC is 30-40 years, and the disease is characterized by life-threatening ventricular arrhythmias in healthy young people [3, 4]. The main goals of anesthesia in patients with ARVC are to maintain hemodynamic stability, minimize stress, and avoid tachycardia, hypertension, and hypotension [5]. Ventricular arrhythmias are exacerbated by β-adrenergic stimulation, whereas α-agonists are less likely to be arrhythmogenic [6]. PSCD can occur at any time in the perioperative period, therefore sympathetic stimulation should be minimized by providing adequate analgesia [5]. We report a case of ARVC managed without ventricular arrhythmias using remimazolam.

2. PRESENTATION OF A CASE

Written informed consent was obtained from the patient for the publication of this case report and the accompanying images. Ethical approval for this study (Nagasaki Rosai No.05001, 2023/04/14) was provided by the Nagasaki Rosai Hospital Institutional Review Board, Sasebo, Japan.

A 51-year-old male patient (weight: 100.1 kg, height:171.0 cm), with a history of ARVC and frequent episodes of stable sustained ventricular tachycardia (VT), underwent open cholecystectomy. He presented to the emergency department with palpitations. He was awake and alert, and his vital signs were otherwise unremarkable.

Electrocardiogram (ECG) showed stable sustained VT with positive QRS in II, III, and aVF, and negative QRS in lead aVL (Fig. 1). This finding is consistent with a left bundle branch block in the inferior axis, as described in the 2010 ARVC Task Force Criteria (Table 1), [7, 8] which requires the presence of epsilon waves (red arrow) at V2 and V3, and inverted T waves at V1, V2, and V3 (Fig. 2). Echocardiography showed a right ventricular fractional area change of 22.43% (Fig. 3). The patient's family history of ARVC was unknown. The patient met the 2010 ARVC Task Force Criteria because three of the major criteria were met [7, 8].

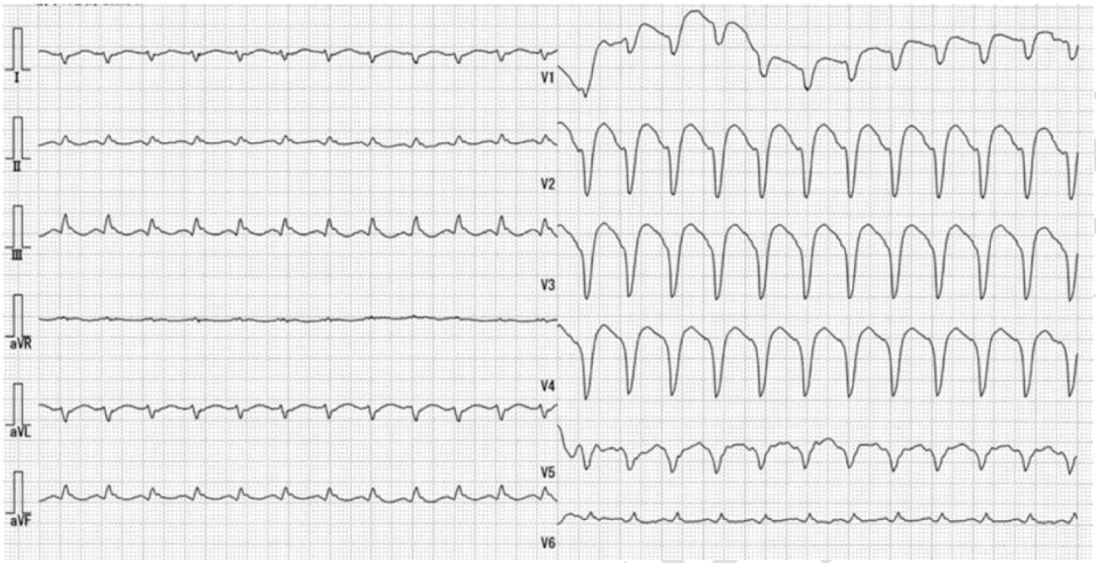

Fig. 1. Stable sustained ventricular tachycardia in the emergency department
The patient presented to the emergency department with palpitations. An electrocardiogram (ECG) showed positive QRS complexes in leads II, III, and aVF, and negative QRS complexes in lead aVL. These ECG findings are consistent with a left bundle branch block in the inferior axis, as described in the 2010 ARVC Task Force Criteria

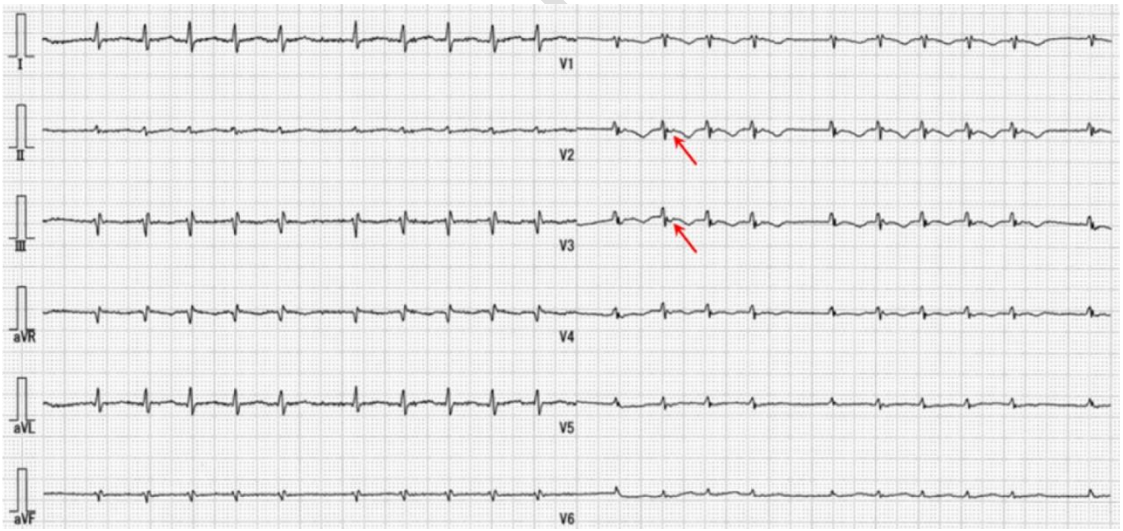

Fig. 2. Preoperative ECG
Epsilon waves (red arrows) are seen in leads V2 and V3, and inverted T waves are seen in leads V1, V2, and V3.

Table 1. 2010 Revised Task Force Criteria for the diagnosis of arrhythmogenic right ventricular cardiomyopathy [7,8]

Modified Task Force Criteria for ARVC – Diagnostic Categories Major and Minor Criteria

Definite: 2 major OR 1 major and 2 minor, OR 4 minor criteria from different categories Borderline: 1 major and 1 minor, OR 3 minor criteria from different categories Possible: 1 major, OR 2 minor criteria from different categories		
	Major	Minor
Global or regional dysfunction and structural alterations determined by echo, MRI, or RV angiography		
Echo	Regional RV akinesia, dyskinesia, or aneurysm and 1 of the following (end diastole): a) PLAX RVOT ≥32 mm (PLAX/BSA ≥19 mm/m^2) b) PSAX RVOT ≥36 mm (PSAX/BSA ≥21 mm/m^2) c) Fractional area change ≤33%	Regional RV akinesia, dyskinesia, or aneurysm and 1 of the following (end diastole): a) PLAX RVOT ≥29 mm to <32 mm (PLAX/BSA ≥16 to <19 mm/m^2) b) PSAX RVOT ≥32 to <36 mm (PSAX/BSA ≥18 to <21 mm/m^2) c) Fractional area change >33 to ≤40%
MRI	Regional RV akinesia or dyskinesia or dyssynchronous RV contraction and 1 of the following a) Ratio RVEDV/BSA ≥110 mL/m^2 (male), ≥100 mL/m^2 (female) b) RVEF ≤40%	Regional RV akinesia or dyskinesia or dyssynchronous RV contraction and 1 of the following: a) Ratio RVEDV/BSA ≥100 to <110 mL/m^2 (male), ≥90 to 100 mL/m^2 (female) b) RVEF >40 to ≤45%
RV angiography	Regional RV akinesia, dyskinesia, or aneurysm	
Tissue characterization of wall		
Endomyocardial biopsy showing fibrous replacement of the RV free wall myocardium in ≥1 sample, with or without fatty replacement and with	Residual myocytes <60% by morphometric analysis (or <50% if estimated)	Residual myocytes 60% to 75% by morphometric analysis (or 50% to 65% if estimated)
Repolarization abnormalities		
ECG	Inverted T waves in the right precordial leads (V1-3) or beyond in individuals >14 years of age (in the absence of complete RBBB QRS ≥120ms)	I. Inverted T waves in leads V 1-2 in individuals >14 years of age (in the absence of complete RBBB) or in V 4-6 II. Inverted T waves in leads V 1-4 in individuals >14 years of age in the presence of complete RBBB
Depolarization/conduction abnormalities		
ECG	Epsilon wave (reproducible low-amplitude signals between the end of the QRS complex to the onset of the T wave) in the right precordial leads (V1-3)	I. Late potentials by SAECG in ≥1 of 3 parameters in the absence of QRS duration of ≥110ms on the standard ECG: a) Filtered QRS duration (fQRS) ≥114 ms b) Duration of terminal QRS <40 μV (low-amplitude signal duration) ≥38 ms c) Root-mean-square voltage of terminal 40 ms ≤20 μV II. Terminal activation duration of QRS ≥55 ms measured from the nadir of the S wave to the end of the QRS, including R' in V 1-3 in the absence of complete RBBB
Arrhythmias		
	Nonsustained or sustained VT of LBBB with superior axis (negative or indeterminate QRS in leads II, III, aVF and positive in lead aVL)	I. Nonsustained or sustained VT or RV outflow configuration, LBBB morphology with inferior axis (positive QRS complexes in leads II, III, aVF and negative in lead aVL) or of unknown axis II. >500 ventricular extrasystoles per 24 hours (Holter)
Family history		
	I. ARVC confirmed in a first-degree relative who meets the current Task Force Criteria II. ARVC confirmed pathologically at autopsy or surgery in a first-degree relative III. Identification of a pathogenetic mutation categorized as associated or probably associated with ARVC in the patient under evaluation	I. History of ARVC in a first-degree relative in whom it is not possible or practical to determine whether the family member meets the current Task Force Criteria II. Premature sudden death (<35 years of age) due to suspected ARVC in a first-degree relative III. ARVC confirmed pathologically or by the current Task Force Criteria in a second-degree relative

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BSA: body surface area; ECG: electrocardiogram; echo: echocardiogram; MRI: magnetic resonance imaging;
PLAX: parasternal long-axis; PSAX: parasternal short-axis; RBBB: right bundle branch block;
RV: right ventricular; RVEDV: right ventricular end-diastolic volume; RVEF: right ventricular ejection fraction;
RVOT: right ventricular out fl ow tract; SAECG: signal-averaged electrocardiogram;
VT: ventricular tachycardia.

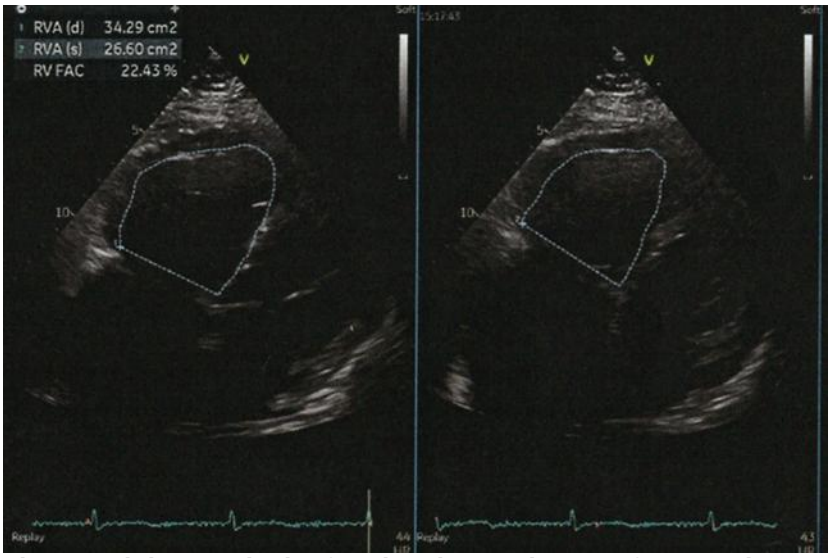

Fig. 3. A right ventricular fractional area change of 22.43% is seen on echocardiography

When the patient presented to the emergency department with a stable sustained VT, procainamide was administered. Afterward, amiodarone was administered due to the persistence of the stable sustained VT. Cardioversion was later required due to the failure of medical therapy to manage his VT.

The patient was treated as if the stable sustained VT occurred during the perioperative period. A defibrillation pad was placed on the patient beforehand. Beta-stimulants are not recommended in the presence of hypotension or bradycardia, because beta-stimulation is the most common cause of stable sustained VT [2, 5, 9]. Based on these considerations, total intravenous anesthesia, mainly remimazolam, was used due to its limited hemodynamic effect.

Phenylephrine and noradrenaline were administered for hypotension, and atropine was administered for bradycardia. General anesthesia was induced with remimazolam (12 mg/kg/h) and fentanyl (500 μg), and tracheal intubation was performed after the administration of rocuronium (1.0 mg/kg). Following intubation, anesthesia was maintained with remimazolam (0.5-1.0 mg/kg/h), remifentanil (0.1-0.2μg/kg/min), rocuronium (7.0 μg/kg/min), and oxygen-in-air gas mixture. The bispectral index was used to titrate the remimazolam dose, which was maintained at 40-60 throughout anesthesia.

After induction of general anesthesia, the modified thoracoabdominal nerves block perichondrial approach (m-TAPA) was done as part of the multimodal analgesia protocol. Levobupivacaine (60 mL, 0.25%) was then administered. Acetaminophen 1000 mg and fentanyl 150 μg were intravenously administered during skin closure. A total of 750μg of fentanyl was administered. Hemodynamic stability was maintained intraoperatively, and catecholamine use was not warranted. The operative time was 154 min and the anesthesia time was 265 min.

The patient was then transferred to the intensive care unit after achieving an appropriate level of consciousness and analgesia. The patient's numerical rating score (NRS) was 0/10 during the first 12 h of follow-up. No analgesic medication was administered within 48 h. No episodes of stable sustained VT or other cardiovascular episodes were observed during the perioperative period. No serious adverse events, such as allergic reactions, local anesthetic systemic toxicity, pneumothorax, or uncontrollable persistent hypotension, were observed.

3. DISCUSSION

Sufficient anesthetic management during an open cholecystectomy of a patient with ARVC, with a history of recurrent stable sustained VT, was achieved. The patient received total intravenous anesthesia with remimazolam, remifentanil, and m-TAPA for postoperative analgesia. Although relatively rare, ARVC may cause sudden, unexpected deaths in the perioperative period [4]. When a β-stimulator is used, ARVC can increase the risk of arrhythmias, such as stable

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sustained VT [2, 10]. Therefore, it is important to maintain hemodynamic stability to avoid fatal arrhythmias during the perioperative period in patients with ARVC [5].

Thiopental has been shown to promote adrenaline-induced arrhythmias; therefore, general anesthesia with propofol or benzodiazepines is preferred [2]. In another report comparing remimazolam and propofol use in cardiac surgery, adrenaline, cortisol, and blood glucose levels measured 2 h after surgery were significantly lower in the remimazolam group. Therefore, remimazolam reduces surgical hemodynamic changes and the surgical stress response [11]. In addition, remimazolam is less likely to cause hypotension and requires less use of beta-stimulators. Therefore, remimazolam may be the best choice for the anesthetic management of ARVC. Remifentanil, fentanyl, and rocuronium were administered safely [4, 9].

α-adrenergic agonists, such as phenylephrine or noradrenaline, are preferred over β-adrenergic stimulators in ARVC patients [2, 5, 9]. In this case, atropine was administered for bradycardia. Postoperative pain is associated with increased levels of endogenous catecholamines, which can lead to severe arrhythmia [2]. However, catecholamine use was not indicated for this patient. M-TAPA was used as postoperative analgesia. With the use of 60 mL of 0.25% levobupivacaine, the pain was NRS 0-1 24 hours after surgery, thus, there was no need for additional analgesics.

Though ARVC appears to be a major cause of sudden and unexpected perioperative death, to our knowledge, there are no published reports on the incidence of ARVC in the perioperative period [4]. A French autopsy report found ARVC in 18 (36%) of 50 sudden perioperative deaths [12]. No preoperative cardiac, intraoperative anesthetic, or surgical complications were observed in the 18 ARVC cases. This autopsy report has some limitations. The percentage of cases in the actual number of anesthesia management cases was not shown, preoperative ECGs were not presented, family history was not described, and there were regional and racial differences in the prevalence of ARVC. Our study report suggests that anesthesiologists should pay special attention to ARVC because of the high risk of VT and sudden death in the perioperative period despite the above-mentioned limitations.

Among the diagnostic criteria for ARVC, the most frequently described ECG finding are T-wave inversions in V1-V3 [13, 14]. T-wave inversion in V1-V3 in those >14 years of age is seen in only 4% of women and 1% of men, and is therefore a useful sign in this patient group [7, 14]. If T-wave inversion is observed in V1-V3 in a young patient, further evaluation, such as echocardiography, may be considered [2, 15]. The epsilon wave observed in this case was inappropriate for screening because it was observed in only 30% of the ARVC patients [16].

A limitation of this case report is that there was only one case. Further research is needed to determine whether remimazolam is the best choice for anesthesia in ARVC patients.

4. CONCLUSION

Although ARVC is a rare heart disease, it may cause sudden death in the perioperative period and should be managed promptly and appropriately. Anesthesiologists should pay close attention to anesthetic management in patients with ARVC. We report a case of ARVC that was safely managed using total intravenous anesthesia with remimazolam.

CONSENT

Written informed consent was obtained from the patient (or other approved parties) for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editorial Office/Chief Editor/Editorial Board members of this journal. Written informed consent for the future publication of this report was obtained from both patients. Informed consent for scientific publication was obtained from the patients.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee, and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. This report has been approved by the Nagasaki Rosai Hospital Institutional Review Board (No.05001, 2023/04/14).

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DEFINITIONS, ACRONYMS, ABBREVIATIONS

ARVC: arrhythmogenic right ventricular cardiomyopathy
VT: ventricular tachycardia
PSCD: perioperative sudden cardiac death
ECG: electrocardiogram
m-TAPA: modified thoracoabdominal nerves block perichondrial approach
NRS: numerical rating scale

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