Adenosine-sensitive incessant right ventricular outflow tract ventricular tachycardia complicating fulminant lymphocytic myocarditis: Case report

Roberto Alvarez Coello, MD, Rodrigo Melo Kulchetscki, MD, Muhieddine Chokr, MD, PhD, Sissy Lara de Melo, MD, PhD, Cristiano Pisani, MD, PhD, Maurício Scanavacca, MD, PhD

From the Arrhythmia Unit, Heart Institute, Hospital das Clínicas, University of São Paulo Medical School, São Paulo, Brazil.

Introduction

Fulminant myocarditis is a rare condition defined as a sudden and severe diffuse cardiac inflammation leading to cardiogenic shock, ventricular arrhythmias, or multiorgan systemic failure.[1] Ventricular tachycardia (VT) may be present in up to 33% of cases of biopsy-proven myocarditis and is associated with increased 90-day mortality.[2]

Mechanisms of VT are not well established but may involve abnormal automaticity.[3] Response to adenosine is described in idiopathic outflow tract VT owing to cyclic adenosine monophosphate (cAMP)-mediated triggered activity,[4] but its effect on myocarditis-induced VT is not well studied.

We report a case of fulminant myocarditis where an incessant monomorphic VT presentation, refractory to antiarrhythmic drugs and direct current cardioversion but with a transitory response to adenosine, was associated with acute hemodynamic deterioration requiring high-dose inotropes and emergency mechanical support.

Case report

A 32-year-old woman, previously healthy except for obesity (body mass index of 43 kg/m^2), was admitted to an emergency department complaining of chest pain that had started 2 days before. She reported a history of a flu-like illness in the past 7 days. An electrocardiogram was performed and showed a nonspecific repolarization abnormality. A marked elevation of cardiac troponin prompted urgent coronary angiography, which showed no obstructive lesions. A diagnosis of myopericarditis was then suggested, and acetylsalicylic acid and colchicine were started.

KEYWORDS Ventricular tachycardia; Abnormal automaticity; Adenosine; Fulminant myocarditis; VA-ECMO
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Address reprint requests and correspondence: Dr Rodrigo Melo Kulchetscki, University of Sao Paulo Heart Institute, Avenia Dr Eneas de Carvalho Aguiar, 44, Instituto do Coração (InCor) - Secretaria da Eletrofisiologia, Laboratório de Hemodinâmica, 2° andar Bloco I, Sao Paulo, Sao Paulo 05403-900, Brazil. E-mail address: r.kulchetscki@gmail.com.

KEY TEACHING POINTS

- Among the multiple possible mechanisms for incessant ventricular tachycardia (VT) in the context of fulminant myocarditis, our case is better explained by abnormal automaticity.
- If adenosine is used on large QRS tachycardia in the context of suspected myocarditis, its effect needs to be interpreted with caution, since transient slowing may happen on automatic VT.
- Mechanical support may have a role for acute VT termination in the context of myocarditis-related cardiogenic shock

Clinical deterioration was followed, and the patient developed heart failure symptoms, hemodynamic instability, and an altered mental status, with the need for orotracheal intubation and vasopressors. Point-of-care echocardiogram showed some degree of left ventricle (LV) dysfunction, so cardiogenic shock was suspected and dobutamine was added. After some clinical stability, she was then referred to our service for evaluation.

At admission, the patient showed a worsening hemodynamic scenario, and a monomorphic incessant VT was detected (Figure 1A). Three direct current cardioversions were performed in a biphasic fashion (100 J, 200 J, and again 200 J) but were unsuccessful in terminating the VT. Slight variations in VT morphology were observed in follow-up electrocardiograms, but the axis was always compatible with a right ventricular outflow tract (RVOT) site of origin. Amiodarone and electrolyte repletion (calcium, magnesium, and potassium) were given, but also without response. An official transthoracic echocardiogram showed a LV ejection fraction (LVEF) of 25% with diffuse biventricular hypokinesia and a paradoxical septal motion.

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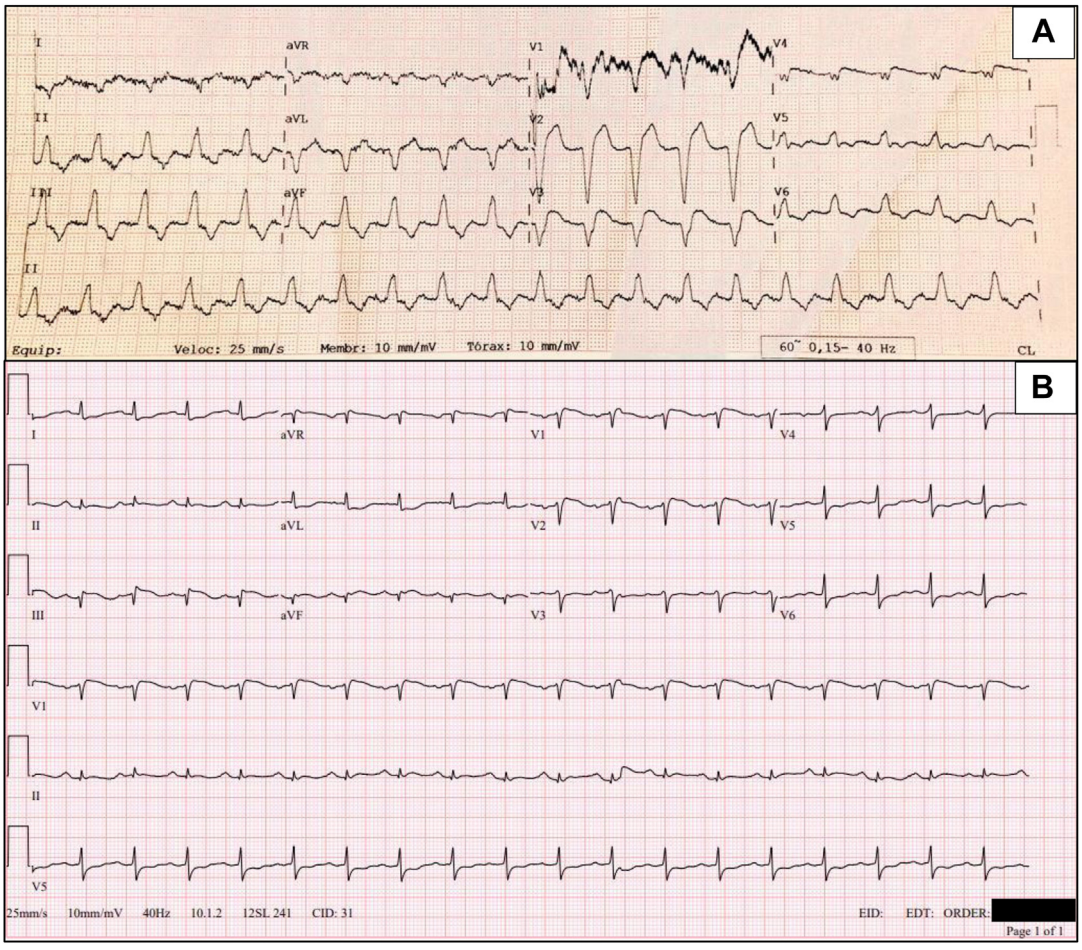

Figure 1 Electrocardiograms of the patient. **A:** Monomorphic ventricular tachycardia with right ventricular outflow tract morphology. **B:** Electrocardiogram in sinus rhythm, showing sinus tachycardia and repolarization abnormalities with minor ST elevation in septal and inferior leads.

It was decided to perform a test with adenosine owing to the site of origin of the VT suggestive of RVOT region. Surprisingly, a change in the rate of the VT and even a momentary reversal to sinus rhythm was observed (Supplemental Video 1).

An emergency electrophysiological (EP) study and VT ablation was suggested, but the patient rapidly progressed to multiorgan dysfunction; venoarterial extracorporeal membrane oxygenation (VA-ECMO) was installed as a bridge to recovery. In a few hours after VA-ECMO, the patient returned to sinus rhythm (Figure 1B).

In addition to LV assist devices, she received pulse therapy with methylprednisolone 1 g/day for 3 days followed by 100 mg/day, as well as intravenous immunoglobulin 30 g/day for 5 days. An endomyocardial biopsy was performed and showed severe lymphocytic myocarditis in the initial stages of organization (Figure 2). Withdrawal of VA-ECMO was achieved after 11 days of admission, with a new echocardiogram showing LVEF 45% in sinus rhythm.

After weaning from VA-ECMO and sedation, some VT was still spontaneously detected, and an EP study was performed eventually. Basic intervals were normal, but despite high-dose isoproterenol (up to 40 mcg in bolus) and programmed ventricular stimulation up to 4 extrastimuli (S4) in 2 different sites in the right ventricle, no arrhythmias were induced (Figure 3). Cardiac magnetic resonance imaging was done 2 months after admission and showed myocardial edema and late enhancement in the inferior basal segment of the LV, with normal chamber diameters but LVEF of 42% and right ventricle ejection fraction of 43%. After some complications such as urinary tract infection, and a careful protocol of weaning immunosuppressive therapy, she was discharged after approximately 2 months of hospitalization with optimized therapy and a planned physical rehabilitation program.

Discussion

Fulminant myocarditis is a rare condition, with a high mortality rate. VT presentation is associated with worse long-term prognosis, as shown in a large Japanese cohort by Kanaoka and colleagues.[2] However, detailed description of VT features, such as most common morphology and response to antiarrhythmic therapies, was not included.

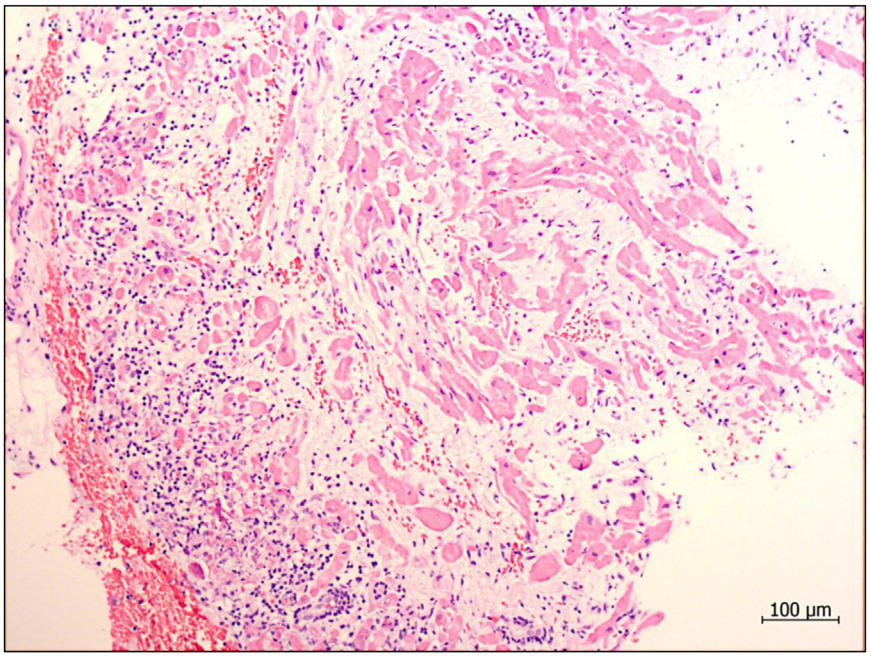

Figure 2 Histological section of the right ventricular septum myocardial sample demonstrating severe lymphocytic inflammatory infiltrates, associated with edema and extensive myocyte damage. The findings are suggestive of a severe lymphocytic myocarditis in the initial stages of organization.

Many different types of ventricular arrhythmias have been described in association with lymphocytic fulminant myocarditis, including incessant VT refractory to electrical cardioversion,[3,5,6] but the mechanism of the arrhythmias remains obscure.

Adenosine is an endogenous nucleoside that has interesting electrophysiologic effects. In the ventricle, it antagonizes the stimulatory actions of catecholamines on calcium inward and on the transient inward currents. This antagonism happens by inhibition of adenylyl cyclase, so adenosine has

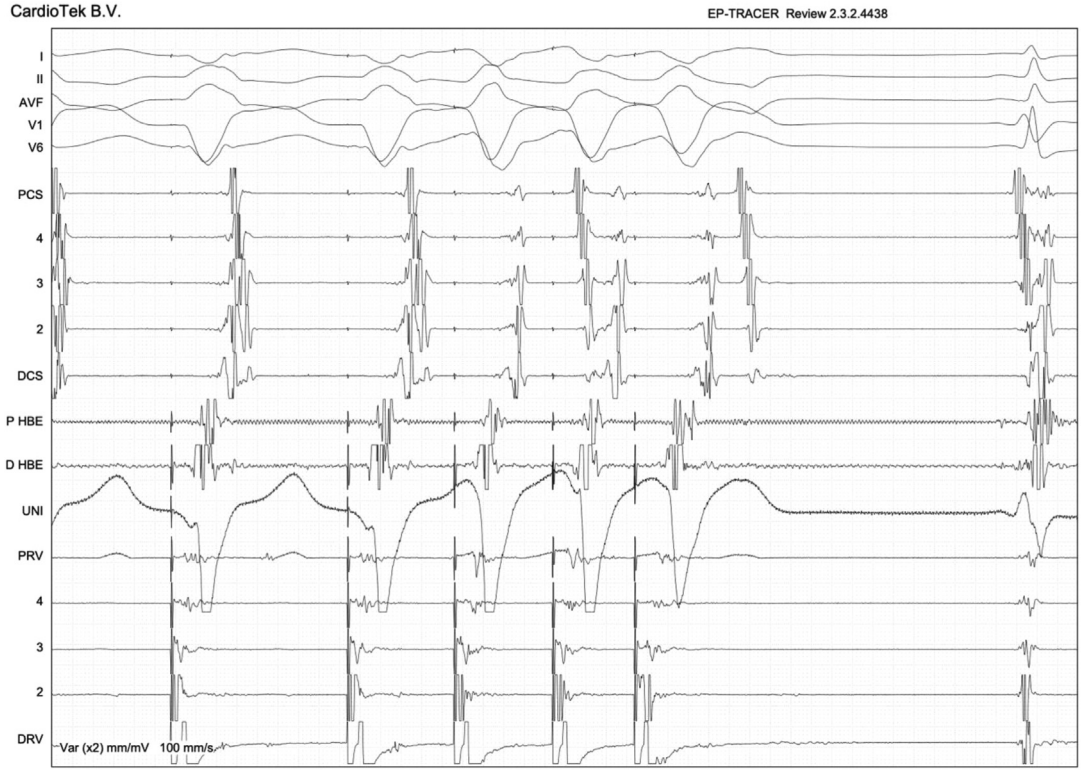

Figure 3 Electrophysiologic study performed days after clinical stability and after weaning from venoarterial extracorporeal membrane oxygenation. Shown here is an example of programmed ventricular stimulation free of ventricular tachycardia induction, even with high-dose isoproterenol and extrastimuli up to S4.

the effect of decreasing the amplitude of delayed afterdepolarizations in scenarios where there is an increase in the concentration of cellular cAMP. Other agents such as verapamil, beta-blockers, or even vagal maneuvers also antagonize the inward calcium current, but more directly, while adenosine does that indirectly, suppressing only cAMP-mediated inward calcium current activation.[7,8] Outflow tract idiopathic VT are classically adenosine sensitive.[4]

As such, in the case of VT, adenosine is successful in terminating cAMP-mediated triggered activity, while it has no effect on other forms of triggered activity. Automatic ventricular arrhythmias may also have a response to adenosine, but they usually are only transiently suppressed (<20 seconds) and never terminated—the mechanism for that suppression is not well described. Macroreentrant VTs, however, are not affected by adenosine infusion.[9]

In our patient, the transient response to adenosine, the refractoriness to repetitive electrical cardioversion, and the fact that, after adequate treatment of the myocarditis with immunosuppressive medications, the EP study could not induce any VT are all compatible with an abnormal automaticity mechanism.

Before the endomyocardial biopsy, however, there was still some doubt regarding the etiology of the myocardial dysfunction, as the VT morphology suggestive of an RVOT origin brought into question if an incessant idiopathic VT-induced ventricular dysfunction could be responsible for such a catastrophic sequence of events. Lerman and colleagues[10] found that adenosine terminated 45 out of 50 focal outflow tract VTs, thus suggesting a cAMP-mediated mechanism. In our case, since the VT was not terminated with adenosine, the hypothesis of abnormal automaticity from the upper right ventricular septum owing to inflammation in the context of a lymphocytic myocarditis is more adequate.

The fact that the cardiac magnetic resonance imaging was done in a convalescent phase of the disease may have underestimated the total myocardial inflammation in the acute phase, and the finding of only a small area of late enhancement in the inferior wall has prognostic implications.[11] The comparative role of VT and the myocardial inflammation in causing acute myocardial dysfunction and cardiogenic shock cannot be accurately determined. Previous studies have shown, however, that correcting sinus rhythm may not be sufficient to restore hemodynamics owing to myocardium instability, and VA-ECMO may improve survival,[12] as was the case in this patient.

Conclusion

Fulminant myocarditis is a rare condition with a poor short-term prognosis that requires urgent acute intervention to increase chances of survival. VT in this condition is associated with even worse outcomes. Mechanisms of incessant VT induced by myocardial inflammation are not well described, but abnormal automaticity may explain the VT mechanism in this case. Studies with a larger number of patients are necessary to better understand the mechanisms of VT, to guide novel therapeutic strategies in this population.

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Appendix

Supplementary Data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hrcr.2023.10.032.

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