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Malignant ventricular arrhythmias during acute infectious illness: mechanisms, mapping, and targeted therapy – illustrative cases

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Abstract

This manuscript presents two cases of life-threatening ventricular arrhythmias occurring during the acute phase of infectious illnesses, emphasizing the role of triggered mechanisms—both early and late—along with Purkinje cell firing and inflammation in arrhythmogenesis. The first case involves a 43-year-old male with hepatitis who developed recurrent monomorphic ventricular tachycardia, exhibiting changing morphologies. The second case describes a 43-year-old male with a febrile illness who presented with recurrent ventricular fibrillation triggered by short-coupled premature ventricular contractions. These cases highlight distinct cellular mechanisms underlying post-infectious arrhythmias and the importance of targeted therapeutic strategies. Key teaching points include the distinction between early afterdepolarization- and delayed afterdepolarization-mediated arrhythmias, the impact of inflammation on arrhythmogenesis, and the utility of advanced mapping and ablation techniques when arrhythmias persist despite initial medical management.

Key words: ventricular arrhythmias, infectious myocarditis, triggered activity, electroanatomical mapping, catheter ablation.

Introduction

Malignant ventricular arrhythmias (VAs) in the setting of acute infectious illnesses, though rare, but life-threatening complications, often associated with myocarditis or myocardial inflammation.

The incidence of ventricular arrhythmias (VA) in myocarditis varies, with up to 25% of patients experiencing arrhythmias during acute myocarditis, primarily in the first 24 hours [1]. Those with sustained ventricular arrhythmias during the acute phase face a high risk of recurrence, with one study showing a 34.8% recurrence rate over a median of 5.5 years [1]. The occurrence and recurrence of VAs are associated with a higher risk of death.

While the link between infections and arrhythmias is well-documented [2], the underlying mechanisms—particularly triggered activity, Purkinje cell involvement, and inflammation—remain poorly understood. This manuscript presents two cases of post-infectious VAs with distinct clinical presentations, diagnostic approaches, and management strategies, providing insights into the pathophysiology, diagnostic challenges, and therapeutic interventions in managing such complex scenarios.

Case Report 1

A 43-year-old male with a history of alcoholism presented with abdominal pain, vomiting, and jaundice. He was diagnosed and treated for hepatitis E. During his hospital stay, he experienced recurrent episodes of broad-complex tachycardia (RBBB morphology) with hemodynamic decompensation (Figure 1A). Initial electrical cardioversion restored sinus rhythm temporarily, but he required an amiodarone infusion and beta-blockers for ongoing arrhythmia (Figure 1B). The QTc interval was recorded as 447 milliseconds in sinus rhythm. Notably, the tachycardia episodes exhibited changing morphologies, transitioning from an initial RBBB pattern to a left bundle branch block (LBBB) pattern with a slower rate (Figure 1C). Coronary angiography revealed normal coronary arteries, while echocardiography showed bi-ventricular systolic dysfunction with a left ventricular ejection fraction (LVEF) of 40%. Cardiac MRI was not performed in this case due to the patient's critical condition; however, given the context of infection and ventricular dysfunction, myocarditis was strongly suspected as the underlying cause. The patient received multidisciplinary care for hepatic impairment and guideline-directed therapy for heart failure. A medically managed 'wait-and-see' approach is often adopted for hemodynamically tolerated VAs in acute, transient inflammatory conditions like myocarditis. However, the persistence of such arrhythmias, even after optimized medical

therapy and resolution of acute sepsis, necessitated consideration for an electrophysiological study (EPS).

During the EPS, tachycardia with a single LBBB morphology was consistently present, with a cycle length of 460 milliseconds. Irregularity in the tachycardia cycle length (TCL) suggested a variable exit from the focal site. After the diagnosis of ventricular tachycardia (VT) was confirmed, Electro-anatomical mapping identified early intracardiac electrograms (EGMs) 30 milliseconds pre-QRS with a QS configuration in the apical right ventricle (Figures 1D-F). Radiofrequency ablation at this site successfully terminated the tachycardia. An isoproterenol infusion did not induce further episodes. Ventricular functions improved significantly at the one-month follow-up, and the patient remained asymptomatic at the two-year follow-up.

Case Report 2

A 43-year-old male with a recent febrile illness experienced a DC shock due to VA. He had a history of chronic hypokalaemia managed with spironolactone therapy. After DC cardioversion, he was started on an amiodarone infusion and referred for further management. Upon admission, he was diagnosed with multiple non-sustained runs of ventricular fibrillation (VF) triggered by short-coupled PVCs. The QTc interval was recorded as 440 milliseconds. Despite supportive treatment, including beta-blockers, lidocaine, and sedatives, the VF persisted (Figure 2A).

Cardiac MRI revealed mild left ventricular dilation with hypokinesis in the mid and basal anterior and anterolateral segments, along with subendocardial oedema predominantly affecting these regions. There was no evidence of late gadolinium enhancement, and the LVEF was measured at 45% (Figure 2D). Coronary angiography showed normal coronary arteries. Despite ongoing antiarrhythmic infusions, the PVCs and VF persisted. Atrial pacing temporarily suppressed the PVCs, but they reappeared upon resuming sinus rhythm.

Electro-anatomical mapping identified intracardiac EGMs occurring 30 milliseconds before the QRS complex with a QS configuration in the basal anterolateral left ventricle (Figures 2B and 2C). Radiofrequency ablation at this site successfully terminated the PVCs. Isoproterenol infusion did not induce further episodes. Postoperatively, the patient was advised corticosteroids, quinidine, and an automated implantable cardioverter-defibrillator (AICD). The decision to implant an AICD was made due to the occurrence of VF and the uncertainty regarding the complete reversibility of the underlying substrate despite successful ablation of

the PVC triggers. Left ventricular function improved, and excellent outcomes were reported at the one-year follow-up.

Discussion

Both cases underscore the role of acute infectious illnesses in creating arrhythmogenic substrates, likely due to transient myocardial inflammation and subsequent remodelling. Reversible ventricular dysfunction may be related to systemic inflammatory states or electrical instability caused by arrhythmia. In Case 2, the short-coupled PVCs triggering VF are highly suggestive of Purkinje system involvement, a known mechanism for VF initiation in various cardiomyopathies and acute inflammatory states. The Purkinje network, with its unique electrophysiological properties, can be particularly vulnerable to changes in calcium handling and sympathetic tone, leading to early afterdepolarizations. While endomyocardial biopsy was not performed in either case, the clinical context, nature of dysfunction, and findings on CMR strongly point towards an inflammatory aetiology. The decision not to perform biopsy was pragmatic, balancing diagnostic yield against patient acuity and the nature of the suspected condition. Non-invasive imaging like CMR provides valuable insights into myocardial oedema and inflammation without the immediate risks of biopsy.

In well-coupled myocardium, a significant depolarizing current is required to overcome the source-sink mismatch to trigger an action potential (AP). However, in myocardium with reduced cell coupling—such as in areas affected by inflammation, fibrosis, or uncoupled gap junctions—the threshold mass of tissue needed to initiate a propagated response decrease [2,3]. Maintaining a critical balance between coupling and uncoupling is crucial, as excessive uncoupling can lead to an unfavourable source-sink match, impairing electrical signal propagation. Cytokine-mediated remodelling of gap junctions and ion channels further contributes to this electrical instability.

Delayed afterdepolarizations (DADs) occur during phase 4 of repolarization and are driven by intracellular calcium overload, typically causing focal monomorphic VT in structurally abnormal myocardium. This mechanism likely explains the arrhythmia in Case 1. Early afterdepolarizations (EADs) arise during phases 2 or 3 of the AP, often due to prolonged repolarization. Factors such as drugs, electrolyte imbalances, or ischemia can influence EADs, potentially leading to polymorphic arrhythmias, or ventricular fibrillation as seen in Case 2. Understanding whether arrhythmias are triggered by EADs or DADs helps guide targeted therapy. DAD-mediated arrhythmias may respond well to agents that stabilize intracellular

calcium handling, while EADs typically require addressing underlying repolarization prolongation [4].

In Case 1, the change in VT morphology could be attributed to a dynamically evolving substrate, multiple foci, or different exit route from the same re-entrant circuit [5,6]. This dynamic nature highlights the challenge of mapping and ablating unstable substrates and supports the need for comprehensive electrophysiological assessment in such cases. Antiarrhythmic drugs, particularly Class I and III agents (e.g., amiodarone), can alter conduction velocity and refractory periods, resulting in changes to the tachycardia cycle length and anisotropic conduction. In Case 2, the patient's long-standing hypokalaemia likely contributed to prolonged repolarization and susceptibility for the VA.

Our clinical management, particularly the decision for early ablation in refractory cases, aligns with current guidelines which recommend catheter ablation for recurrent, symptomatic VT/VF refractory to medical therapy, even in the setting of acute myocarditis where a "wait-and-see" approach for spontaneous resolution is often considered first for hemodynamically stable arrhythmias. The persistence of severe, life-threatening arrhythmias despite optimal medical management and resolution of the acute infection justified an invasive approach in both instances, providing rapid and sustained arrhythmia control.

Implications and future directions

These two cases, while well-described, have limited generalizability due to their small number. However, these cases provide practical insights for clinicians managing post-infectious VAs. A systematic approach, including prompt identification of triggers (e.g., short-coupled PVCs), advanced imaging like CMR for myocardial inflammation, and electrophysiological studies for refractory arrhythmias, is crucial. In settings of acute inflammation, initial management often involves antiarrhythmics, electrolyte correction, and addressing the underlying infection. However, when VAs persist and pose a life-threatening risk, as in our cases, early consideration of catheter ablation of focal triggers can be life-saving. The choice between a wearable cardioverter-defibrillator (WCD) and an AICD should be individualized, weighing the potentially transient nature of the arrhythmogenic substrate against the severity of the arrhythmia and the potential for recurrence.

Conclusions

These cases illustrate the complex relationship between acute infectious diseases and malignant VAs, emphasizing the need to consider transient inflammatory processes like myocarditis in such scenarios. They highlight the diagnostic challenges, the distinct cellular mechanisms (EADs vs. DADs, Purkinje involvement), and the critical role of advanced electrophysiological techniques for effective management when arrhythmias are refractory to conventional therapies.

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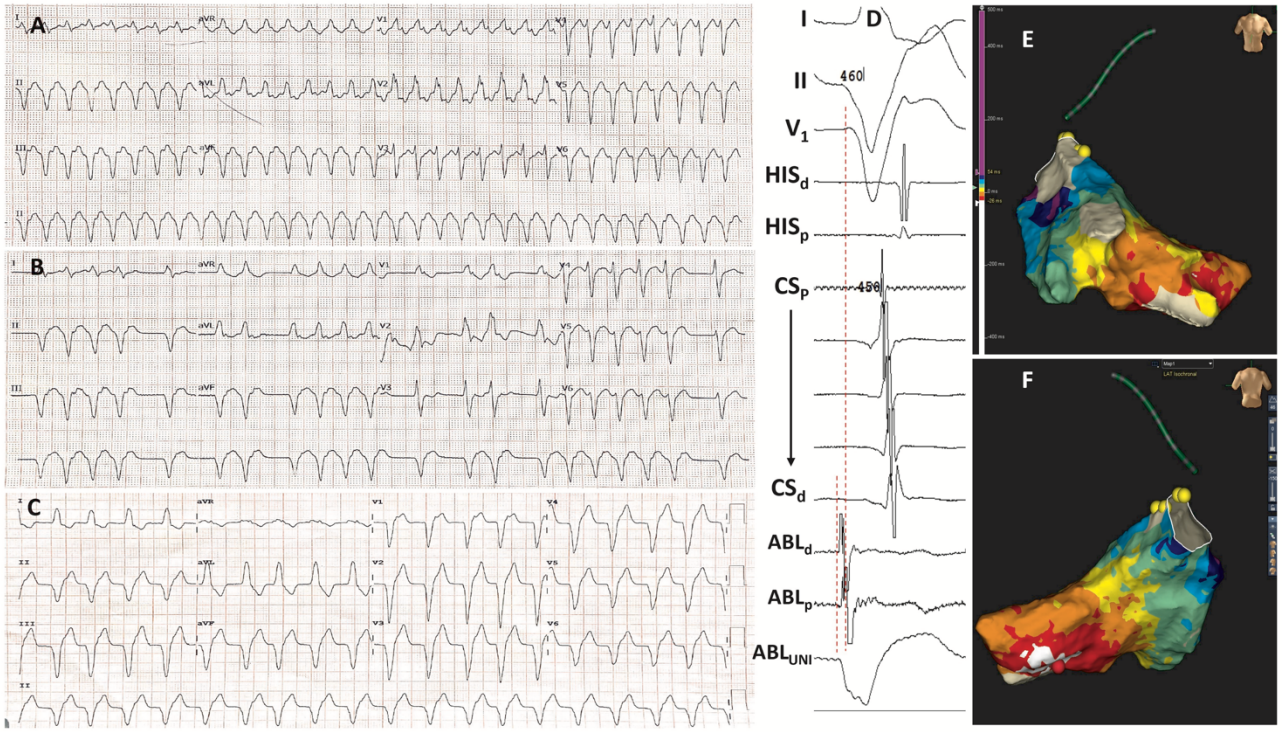

Figure 1. A) Fast broad complex tachycardia; B) tachycardia with similar morphology but with a variable cycle length and a right bundle branch block (RBBB) pattern; C) regular, slow broad complex tachycardia and a left bundle branch block (LBBB) pattern; D) local intracardiac electrograms showing a pre-QRS interval of -30 ms and a QS configuration in unipolar ablation; E,F) 3D activation map that localizes the tachycardia to the right ventricular apex, where ablation successfully terminated the arrhythmia.

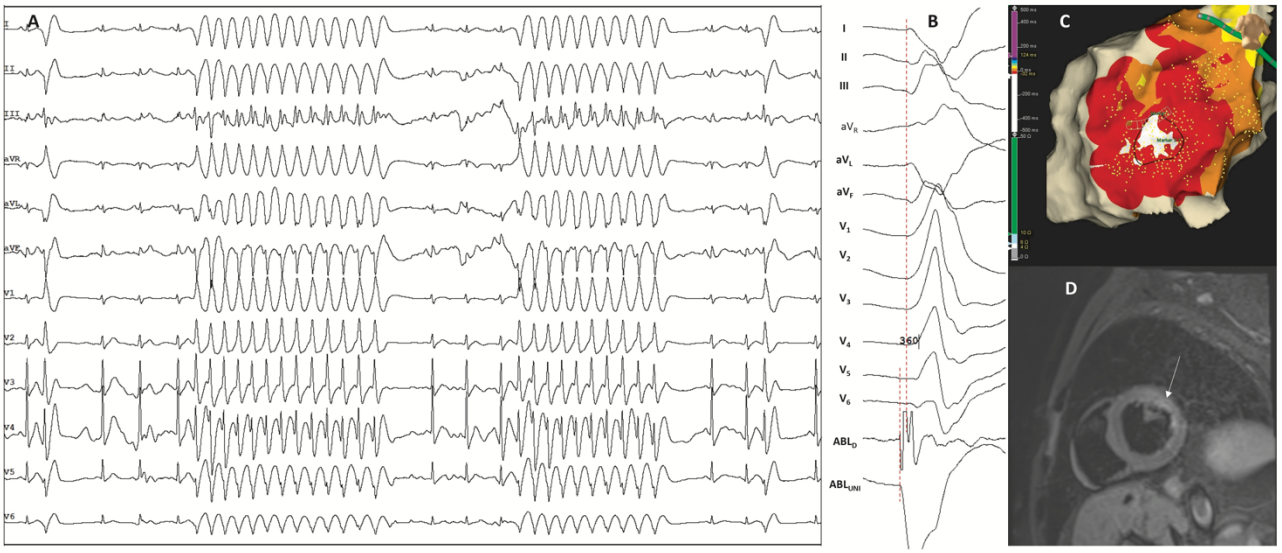

Figure 2. A) Sinus rhythm with short-coupled PVCs initiating non-sustained runs of malignant ventricular arrhythmia; B) local intracardiac electrograms showing a pre-QRS interval of -30 ms and a QS configuration in unipolar ablation; C) 3D electro-anatomical map localising the PVC/VT focus to the basal anterolateral left ventricle; D) T2-weighted MRI displaying subendocardial oedema predominantly affecting the anterolateral left ventricle, corresponding to the area identified on the 3D map.