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Case Report

Bidirectional Ventricular Tachycardia in a Patient With Fulminant Myocarditis Secondary to Cardiac Sarcoidosis Mimicking Giant Cell Myocarditis

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ABSTRACT

Differentiating between sarcoidosis and giant cell myocarditis (GCM) based on clinical presentation is difficult. We present the case of a 57-year-old woman who was initially diagnosed with GCM based on endomyocardial biopsy. The patient was refractory to standard management for GCM and went on to develop bidirectional ventricular tachycardia, a finding suggestive of sarcoidosis. Unfortunately, the patient eventually needed cardiac transplantation. The explanted heart demonstrated cardiac sarcoidosis. Bidirectional ventricular tachycardia has not been demonstrated in GCM, and its presence may help in distinguishing between GCM and cardiac sarcoidosis.

RÉSUMÉ

La distinction entre la sarcoïdose et la myocardite à cellules géantes (MCG) fondée sur le tableau clinique est difficile. Nous présentons le cas d'une femme de 57 ans qui avait initialement reçu un diagnostic de MCG à la suite de la biopsie endomyocardique. Comme la MCG diagnostiquée chez la patiente était réfractaire à la prise en charge thérapeutique habituelle, elle a continué à souffrir de tachycardie ventriculaire bidirectionnelle, un signe évocateur de sarcoïdose. Malheureusement, la patiente a finalement eu besoin d'une transplantation cardiaque. Le cœur explanté a démontré une sarcoïdose cardiaque. Bien que la tachycardie ventriculaire bidirectionnelle n'ait pas été démontrée lors de MCG, sa présence peut aider à distinguer la MCG de la sarcoïdose cardiaque.

Case

A 57-year-old previously healthy woman presented initially to a community hospital complaining of exertional chest discomfort and was labeled as having an acute coronary syndrome characterized by troponin elevation in the context of a left bundle branch block on her electrocardiogram (Fig. 1A), with no prior studies for comparison. Coronary angiography demonstrated normal coronary arteries. Echocardiography demonstrated left ventricular systolic dysfunction with an ejection fraction of 33% and mild ventricular dilatation (left ventricular end-diastolic diameter: 5.8 cm). Severe hypokinesis of the mid to basal septum and mild mitral regurgitation were described. She was started on an angiotensin-converting enzyme inhibitor and beta blocker, and then discharged home.

Eleven days post-discharge, the patient developed syncope while driving, resulting in a motor vehicle accident. She was admitted to our institution for further workup and observation and was otherwise initially asymptomatic. Her electrocardiogram was unchanged, and her telemetry revealed no malignant arrythmias for the first week of her admission. Her initial troponin level was elevated, at 899 ng/L (by high-sensitivity troponin-T test; normal high $\leq$ 14), and it peaked at 1061 ng/L. It stayed persistently elevated ($>$ 800 ng/L) for over 2 weeks following her admission. Her echocardiogram demonstrated more-extensive wall motion abnormalities, with an ejection fraction of 25%-30% and akinesis of the mid to basal segments of the septum, lateral wall, and anterior and inferior walls, along with moderate-to-severe mitral regurgitation (Videos 1-4, view videos online). She underwent cardiac magnetic resonance imaging on the sixth day of her admission, which revealed multiple left ventricular wall segments of diffuse hyperintense signal on the triple inversion recovery T2-weighted images, suggestive of acute/subacute myocardial edema. Areas of transmural and subepicardial delayed enhancement involving the

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Novel Teaching Points

- GCM and CS are distinct entities, with significant overlap, and misdiagnosis is not uncommon. EMB should be performed when possible. Pathology should be reevaluated from other sources, including explanted hearts and left ventricular assist device core biopsy samples.
- Bidirectional VT is a unique arrhythmia that has been described as linked to cardiac sarcoid. Clinically, the presence of this arrhythmia may help in distinguishing CS from GCM.
- Lidocaine may be a better treatment option for bidirectional VT, given the pathophysiology of this arrhythmia.

interventricular septum were noted, suggestive of scarring in the setting of prior myocarditis (Supplemental Fig. S1).

Seven days following her admission, she became dyspneic and demonstrated clinical evidence of worsening heart failure that required intravenous diuretics and inotropic support with milrinone and nitroprusside. She underwent right heart catheterization and endomyocardial biopsy (EMB). Right heart catheterization revealed mild pulmonary hypertension, with a mean pulmonary artery pressure of 28 mm Hg, an elevated wedge pressure of 24 mm Hg, and low cardiac index (Fick cardiac index of 1.87 L/min per m^2; thermodilution cardiac index of 2.0 L/min per m^2), consistent with cardiogenic shock. Seven biopsy samples were obtained, and the histopathology results revealed lymphohistiocytic myocarditis with giant cells. There was multifocal myocarditis in a patchy distribution in most pieces. Histiocytes were the predominant inflammatory cells, and there were frequent multi-nucleated giant cells (Fig. 2A). There were also frequent lymphocytes, plasma cells, and eosinophils. The inflammation was associated with myocardial damage. There was no evidence of granulomas, vasculitis, or caseous necrosis, and stains were negative for acid fast bacilli and fungus. These findings were felt to be most suggestive of giant cell myocarditis (GCM), and the patient was promptly started on immunosuppressive therapy with cyclosporine, pulsed intravenous steroids with methylprednisolone (later switched to oral prednisone), and mycophenolate mofetil. Additionally, she received 3 doses of intravenous immunoglobulin.

Shortly after treatment with immunosuppressive therapy, the patient developed ventricular arrythmias that were felt to be out of keeping with her inotrope doses, and her filling pressures. Initially, there was noted frequent ventricular ectopy and runs of nonsustained ventricular tachycardia (VT) that progressively became more sustained VT. The ectopy and monomorphic VT were of 2 predominant morphologies: right bundle left superior axis (Fig. 1B) and right bundle right inferior axis (Fig. 1C). The runs of VT were initially monomorphic, then interestingly became bidirectional (Fig. 1D). The alternating QRS morphologies matched the 2 initial monomorphic VTs. Her VT was refractory to intravenous

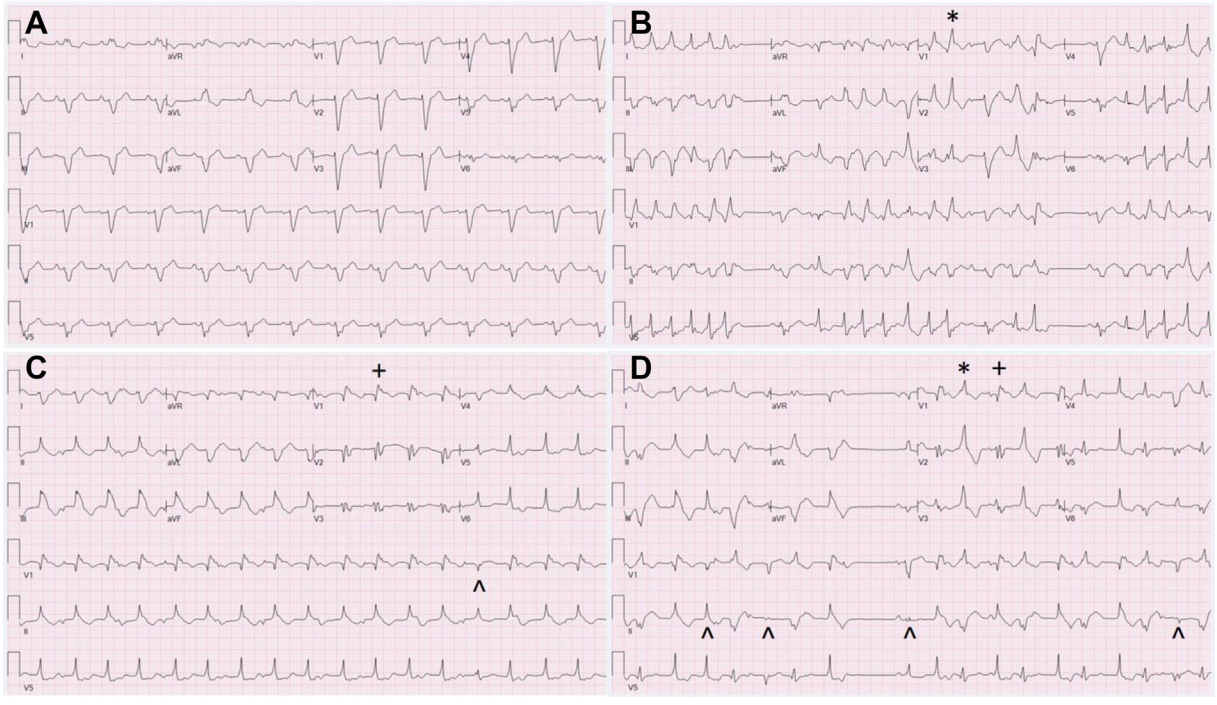

Figure 1. Progression to bidirectional ventricular tachycardia: (**A**) Baseline electrocardiogram upon admission to hospital shows sinus rhythm with a left bundle branch block and left-axis deviation. (**B**) Recurrent runs of nonsustained monomorphic ventricular tachycardia first morphology (VT1) (*) (—right bundle left superior axis) with atrioventricular (AV) dissociation. (**C**) Sustained monomorphic ventricular tachycardia second morphology (VT2) (+) (right bundle right inferior axis) with AV dissociation, and a fusion beat (^). (**D**) Recurrent runs of bidirectional ventricular tachycardia with the alternating morphologies matching prior VT1 (*) and VT2 (+) and with AV dissociation with various capture and fusion beats (^).

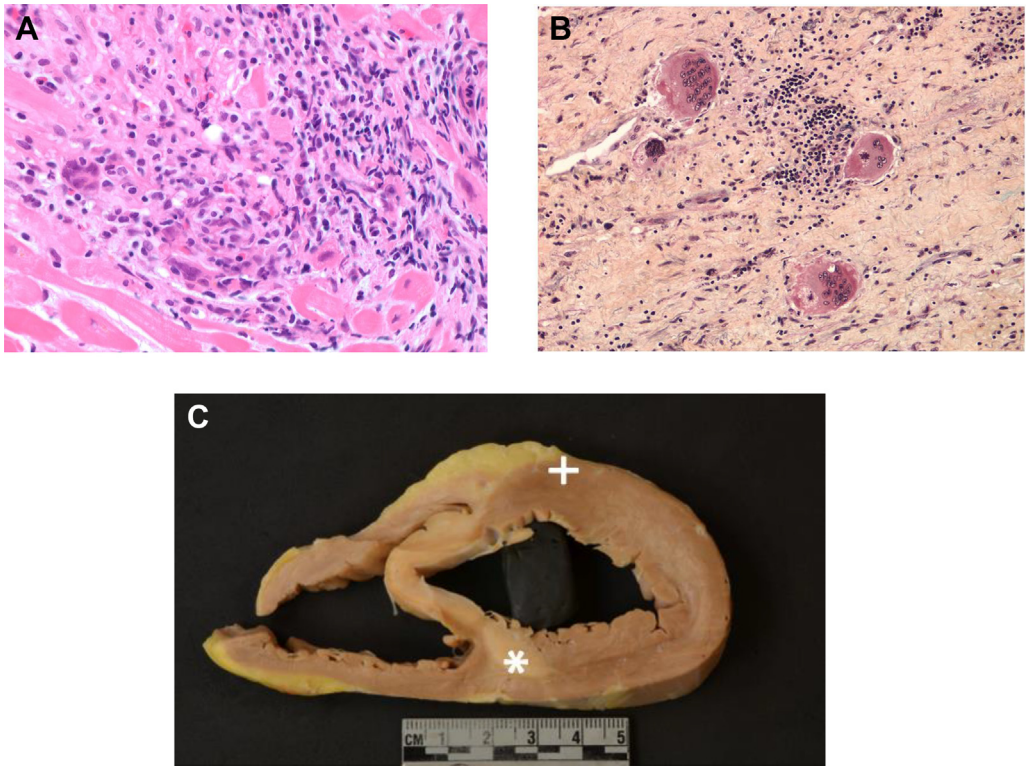

Figure 2. (**A**) Multifocal myocarditis: Shown is a microscopic presentation of endocardial biopsy from our patient showing multifocal myocarditis with multi-nucleated giant cells and many inflammatory cells, including lymphocytes, plasma cells, and eosinophils. (**B**) Granulomatous inflammation: Shown is a microscopic presentation of the pathologic analysis of the explanted heart—well-formed granulomas with asteroid bodies consistent with a diagnosis of cardiac sarcoidosis. (**C**) Gross cross-sectional pathology of explanted heart: clear scar can be seen at the basal left ventricular septum, extending from the posterior wall to the anterior wall, with proposed exit sites of ventricular tachycardia first morphology (VT1) (*), inferoseptal basal left ventricle, and ventricular tachycardia second morphology (VT2) (+) anterolateral basal left ventricle.

amiodarone, which was initially bolused and infused with doses of 900-1400 mg per day. The VT appeared to be more responsive to lidocaine intravenous boluses of 75-100 mg, in addition to an infusion starting at 0.5-1 mg/min, but required up-titration to higher doses of 2-3 mg/min, which were not tolerated by the patient due to headaches and confusion. The patient underwent repeat EMB 14 days following her initial biopsy, to assess her histologic response to immunosuppression. Biopsy samples showed foci of chronic lymphohistiocytic inflammation with occasional eosinophils, with associated fibrosis, and hemosiderin deposits; no giant cells or granulomas were identified. The pathology impression was that there had been histologic improvement.

Despite the pathology findings, the patient remained clinically labile, with refractory heart failure and ongoing ventricular arrythmias with evidence of fulminant myocarditis. She was ultimately listed for cardiac transplantation with urgency (Canadian Cardiovascular Society status 3.5) and underwent orthotopic cardiac transplantation 34 days after her admission to our institution. She required extracorporeal membrane oxygenation immediately post-transplantation, owing to acute deterioration in right ventricular function in the donor heart. The patient gradually improved, requiring a prolonged admission post—cardiac transplantation, but she was eventually discharged from the hospital in stable condition. Pathologic analysis of her explanted (native) heart showed regional scarring, well-formed granulomas, asteroid bodies, and a lack of organisms consistent with a diagnosis of cardiac sarcoidosis (CS; Fig. 2, B and C).

Discussion

GCM and CS have many similarities, which can be a challenge for clinicians. Both are believed to be related to T-cell activation. GCM is characterized by multinucleated giant cells with diffuse myocardial inflammation and necrosis. Noncaseating granulomas have been the pathologic hallmark of CS. Both diseases clinically can result in heart failure, ventricular arrhythmias, and conduction disease. GCM can result in rapid deterioration clinically, with impending death.[1] In this case, the final diagnosis was made with examination of the explanted heart. There are several salient learning points from this case—there is a need for both EMB and follow-up pathology from the transplanted heart, and the arrythmia that has been linked to CS has a unique nature.

EMB is indicated for patients with suspected GCM, given the potential for tailored immunosuppressive, cyclosporine-based therapy and for rapid clinical decline if left untreated. The sensitivity of EMB for GCM ranges from 68% to 80%.[2] However, biopsy has a demonstrated lower sensitivity for CS (35%), likely owing to the patchy nature of its distribution within the left ventricle. Prior treatment with steroid therapy,

and/or inadequate sampling, may be additional factors contributing to a false-negative biopsy result for CS. The hallmark of GCM are "giant cells" pathologically referring to CD68+ macrophages found at the borders of myocardial necrotic areas. When giant cells are absent, misdiagnosis trending toward lymphocytic myocarditis may occur.[3] Similarly, the absence of granulomas and fibrosis demonstrated on EMB may lead to a misdiagnosis favouring GCM when in fact CS is present. A recently published large retrospective study from Finland examined 73 cases of GCM diagnosed since the late 1980s and re-examined all available histologic material used in making the initial diagnosis.[4] The majority of cases (62%) initially diagnosed as GCM were reclassified as CS; most of the misdiagnoses were due to granulomas being missed or misinterpreted. Histologic samples may have included follow-up biopsies, explanted or autopsied hearts, or autopsy of extracardiac tissues. Imaging studies using fluorodeoxyglucose positron emission tomography were also used when possible. For our patient, fluorodeoxyglucose positron emission tomography was not readily available, given the critically ill nature of the patient and the need for urgent advanced medical therapies.

Ventricular arrythmias may occur in patients with either GCM or CS, but the presence of bidirectional VT may have been a clue that the patient was more likely to have sarcoidosis. Bidirectional VT is a rare rhythm that classically has been associated with digoxin toxicity and catecholaminergic polymorphic VT. Mechanistically, it requires 2 different sites in the distal His-Purkinje system or ventricular myocardium where delayed afterdepolarization (DAD)-triggered activity develops at different heart-rate thresholds. The second site develops ventricular bigeminy and activates the first site by a "ping-pong" mechanism,[5] resulting in reciprocating bigeminy and the specific pattern of alternating axis and morphology of the VT. Bidirectional VT in CS has been reported in the literature in a single case report by Benjamin et al., who hypothesized that the arrythmia may be due to scar-mediated reentry around a circuit with 2 different alternating paths for exit.[6] Bidirectional VT has also been described in fulminant myocarditis, but never in GCM, which is characterized by several ventricular arrythmias, most commonly monomorphic VT.[7,8]

In our particular case, the electrocardiogram evidence favours a DAD-mediated mechanism over a mechanism of macro-reentry with alternate exit sites. Although the pathology on the explanted heart (Fig. 2C) demonstrated a prominent scar in an area of the left ventricle consistent with the likely exit sites of the 2 VT morphologies (basal anterolateral left ventricle and basal inferoseptal left ventricle), this does not argue against a DAD-mechanism, which occurs more commonly in injured myocardial tissue. Arguing for a DAD-mediated mechanism are the presence of both QRS morphologies commonly seen in the patient, with runs of monomorphic VT, as well as isolated ectopy. These would be less likely to be seen with a macro-reentry mechanism. In addition, the monomorphic VT (Fig. 1C) has a longer cycle length than the coupling interval between the 2 QRS morphologies (Fig. 1D). With a macro-reentry mechanism, this finding would be challenging to explain other than by variable effects of anti-arrhythmic medications on the 2 electrocardiograms. Finally, our patient demonstrated arrhythmia suppression with lidocaine, more so than with amiodarone. Lidocaine can inhibit DAD-related trigger activity and suppress excitability through the blocking of voltage-gated sodium channels in cardiac myocytes.

The presented case highlights the diagnostic dilemma posed by GCM and CS. Bidirectional VT, although traditionally associated with digoxin toxicity and catecholaminergic polymorphic VT, has been reported with CS and other myocardial inflammatory diseases, but not with GCM. Thus, although the literature evidence is currently sparce for a relatively rare entity, the presence of bidirectional VT should cause the clinician to consider the diagnosis of CS over GCM in the context of myocarditis.

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Disclosures

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Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2021.07.007.